Estrogen Report

OPTIMAL HEALTH FOR LIFE

GENE MATRIX

GENOTYPE REPORT

NAME	NGx Sample
DATE OF BIRTH	1/1/1900
REFFERRING PRACTITIONER	
DATE REPORTED	2/20/2023 11:29:08 AM
ACCESSION NUMBER	DNA013992ZA

WELCOME TO YOUR DNA ESTROGEN REPORT

From your buccal swab sample we have used a process called the Polymerase Chain Reaction (PCR), which copies the DNA of your genes many times over so that we can generate sufficient quantities to analyze your genetic material. Then, we identify unique DNA sequences in some of your genes.

Considerable inter-individual variability has been observed in biological areas that are involved in carcinogen metabolism, metabolism of steroid hormones, and phase I and phase II detoxification. Variations in genes involved in these biological processes help identify a sub-population of women and men with higher lifetime exposure to estrogens, estrogen metabolites and other carcinogens. Understanding an individual's genetic variability will allow for targeted diet, lifestyle and hormone intervention.

HOW TO READ YOUR RESULTS

You will find your genetic results in the following pages. On the left side, you will see the gene name and description. On the right side, you will find your specific result and an explanation of the results, associated risks, and diet and lifestyle recommendations. Please see the key above to identify each impact level.

NO IMPACT
Genotype has no effects on the biological area in question.

LOW IMPACT
Genotype has mild effects on the biological area in question with a small change in responsiveness to environmental influences.

MODERATE IMPACT
Genotype has moderate effects on the biological area in question. Attention should be paid, and some dietary and lifestyle changes are recommended.

HIGH IMPACT
Genotype has significant impact on the biological area in question. Cohesive and intensive diet and lifestyle action should be taken.

SUMMARY OF YOUR RESULTS

The combination of gene variants identified in this analysis indicates possible inefficiencies in estrogen detoxification, and additional support would be recommended.

AREA OF ACTIVITY	GENE	GENETIC VARIATION	RESULT	GENE IMPACT
Detoxification Oestrogen	CYP17A1	-34T>C	A/G	
	CYP1A1	Msp1 T>C	T/T	
		2454A>G (Ile462Val)	T/T	
	CYP1B1	4326C>G (Val432Leu)	C/G	
	GSTM1	519G>C	G/G	
	GSTT1	15G>C	C/C	
	NQO1	609C>T	C/C	
	SULT1A1	638G>A	A/A	
Methylation Oestrogen	COMT	472G>A (Val158Met)	A/G	
	MTHFR	677C>T	AA	
Oxidative Stress Oestrogen	SOD2	-28C>T (Ala16Val)	C/C	
Thrombosis	F5	G1691A	CC	

TEST RESULTS

F5 | G1691A

Factor V functions as a cofactor to allow factor Xa to activate the enzyme thrombin, and in turn cleaves fibrinogen to form fibrin, which polymerizes to form the dense meshwork that makes up the majority of a clot. Activated protein C (APC) is a natural anticoagulant that acts to limit the extent of clotting by cleaving and degrading factor V. Factor V Leiden gene mutation is characterized by a poor anticoagulant response to APC and an increased risk for venous thromboembolism (VTE). Deep venous thrombosis (DVT) is the most common VTE, with the legs being the most common site. However, VTE can also occur in other parts of the body including the brain, eyes, liver, and kidneys.

YOUR RESULT: **CC**

No variant was detected at the 1691 G>A (C>T) locus.

MTHFR | 677C>T

Methylenetetrahydrofolate Reductase (MTHFR) is a key enzyme in the folate metabolic pathway and the multistep process that converts the amino acid homocysteine to methionine. Methionine is used to in the synthesis of proteins and other important antioxidant compounds involved in detoxification of estrogens. Reduced activity influences the balance between DNA synthesis, repair and methylation processes.

YOUR RESULT: **AA**

The T allele lowers activity of the MTHFR enzyme, which results in an increase in homocysteine levels, a decrease in DNA methylation and an increase in DNA adducts. Decreased MTHFR enzyme activity has been associated with detrimental effects of long term exposure to estrogens. These individuals have increased folate, vitamin B2, B6 and B12 requirements. In addition to ensuring folate-rich foods, a general B vitamin or multi-vitamin supplement containing as much as 800ug folate may be recommended.

COMT | 472G>A (Val158Met)

Soluble catechol-O-methyltransferase (S-COMT) helps control the levels of certain hormones and is involved in methylation and inactivation of catechol estrogens. Accumulation of some estrogen metabolites, which leads to oxidative DNA damage, is a recognized risk factor for of breast cancer.

YOUR RESULT: **A/G**

The A allele is associated with a 3-4 fold reduction in the methylation activity of the COMT enzyme. For A allele carriers, beneficial modulation of estrogen metabolism can be accomplished through dietary and lifestyle modifications. Key interventions include increasing insoluble fiber, managing the quality of dietary fat intake, increasing phytoestrogen intake, losing weight, and increasing exercise. In addition, select nutrients and micronutrients effectively reduce estrogen load by supporting preferred estrogen pathways. These are included at the end of the report.

CYP1A1 | Msp1 T>C

The CYP1A1 gene encodes a phase I cytochrome P450 enzyme that converts environmental procarcinogens such as polycyclic aromatic hydrocarbons (PAHs) and aromatic amines to reactive intermediates having carcinogenic effects. In addition, CYP1A1 is involved in the oxidative metabolism of estrogens, which may play a critical role in the etiology of breast and prostate cancers. CYP1A1 enzyme catalyzes the 2-hydroxylation of estradiol (E1 and E2) in several extra hepatic tissues including breast tissue. It is also involved in activating cigarette smoke, diet and environmental pollutants, as well as producing carcinogens.

YOUR RESULT: **T/T**

No variant was detected at the Msp1 T>C locus.

CYP1A1 | 2454A>G (Ile462Val)

The CYP1A1 gene encodes a phase I cytochrome P450 enzyme that converts environmental procarcinogens such as polycyclic aromatic hydrocarbons (PAHs) and aromatic amines to reactive intermediates having carcinogenic effects. In addition, CYP1A1 is involved in the oxidative metabolism of estrogens, which may play a critical role in the etiology of breast and prostate cancers.

YOUR RESULT: **T/T**

No variant was detected.

CYP17A1 | -34T>C

CYP17 mediates both steroid 17a-hydroxylase and 17, 20-lyase activities, and catalyzes a rate-limiting step in ovarian and adrenal biosynthesis leading to the precursor, dehydroepiandrosterone. The C allele increases enzyme activity, thereby increasing the amount of bioavailable estrogen.

YOUR RESULT: **A/G**

For individuals with the C (G) allele, beneficial modulation of estrogen metabolism can be accomplished through dietary and lifestyle modifications. Key interventions include increasing insoluble fiber, avoiding refined carbohydrates, increasing phytoestrogen intake, losing weight, and increasing exercise. In addition, select nutrients and micronutrients effectively reduce estrogen load by supporting preferred estrogen pathways. These are included at the end of the report.

CYP1B1 | 4326C>G (Val432Leu)

CYP1B1 enzyme catalyzes the 4-hydroxylation of estradiol; it also oxidizes a variety of procarcinogenic compounds to their activated forms, including polycyclic aromatic hydrocarbons (PAHs) and arylamines.

YOUR RESULT: **C/G**

This SNP has been found to have the most profound impact on the catalytic properties of CYP1B1, with the 4 -hydroxylase activity of the G allele displaying three-fold higher activity compared to the C allele. In the presence of the G allele, it is important to reduce exposure to all diet and environmental procarcinogens such as PAH, aromatic amines, nitrates, and smoking of any kind. In addition, attention should be paid to optimizing phase 2 detoxification.

GSTM1 | 519G>C

Glutathione S-transferase M1 is the most biologically active member of the GST super-family and is involved in Phase II detoxification in the liver. It is responsible for the removal of xenobiotics, carcinogens, and products of oxidative stress. These enzymes are involved in the phase 2 conjugation of estrogen quinones to glutathione.

YOUR RESULT: **G/G**

This genotype indicates the presence of the GSTM1 gene.

GSTT1 | 15G>C

Glutathione S-transferases (GSTs) are a family of multifunctional enzymes involved in the metabolism of a variety of xenobiotic compounds, including mammary carcinogens. These enzymes are involved in the conjugation of estrogen quinones to glutathione.

YOUR RESULT: **C/C**

This genotype indicates the presence of the GSTT1 gene.

NQO1 | 609C>T

NADP(H:) quinone oxidoreductase 1 (NQO1) often referred to as Quinone Reductase is primarily involved in the detoxification of potentially mutagenic and carcinogenic quinones derived from tobacco smoke, diet and estrogen metabolism. NQO1 also protects cells from oxidative stress by maintaining the antioxidant forms of ubiquinone and vitamin E.

YOUR RESULT: **C/C**

The analysis identified no genetic variation at the 209 C>T locus.

SULT1A1 | 638G>A

Sulfotransferase 1A1 (SULT1A1) is involved in the inactivation of estrogens and bio-activation of heterocyclic amines and polycyclic aromatic hydrocarbons.

YOUR RESULT: **A/A**

A allele carriers have a substantially lower activity of this enzyme, which has been associated with increased with higher BMI, and longer exposure to endogenous hormones. For individuals with the A allele, beneficial modulation of estrogen metabolism can be accomplished through dietary and lifestyle modifications. Key interventions include increasing insoluble fiber, avoiding refined carbohydrates, increasing phytoestrogen intake, losing weight, and increasing exercise. In addition, select nutrients and micronutrients effectively reduce estrogen load by supporting preferred estrogen pathways. These are included at the end of the report.

SOD2 | -28C>T (Ala16Val)

The SOD2 gene encodes the superoxide dismutase 2, a mitochondrial enzyme involved in the elimination of free radicals which are normally produced within cells and which are damaging to biological systems. The enzyme thus has important antioxidant activity within the cell, especially within the mitochondria.

YOUR RESULT: **C/C**

Individuals with the C allele and with a lower consumption of fruits and vegetables may have an increased risk of experiencing the damaging effects of oxidative stress resulting from free radicals. These effects are also enhanced by the presence of additional risk factors such as smoking or the use of hormone replacement therapy. Therefore, it is important for individuals with the C allele to ensure adequate fruit and vegetable intake. Supplementation with antioxidant nutrients can also reduce the oxidation of catechols and promote greater excretion of these metabolites through the methylation pathway.

NUTRITION AND ESTROGEN

If a moderate or high impact gene variant is present for COMT, SULT1A1 or CYP17A, the following nutritional support is recommended to effectively reduce estrogen load while supporting preferred estrogen pathways:

• For breakdown of estrogen to the beneficial 2-OH metabolite, supplement with a bio-available form of 3,3'-Diindolylmethane (DIM), or substantially increase intake of cruciferous vegetables (cauliflower, broccoli, cabbage, brussels sprouts).

• Include phytoestrogens in the diet for their many beneficial influences on estrogen synthesis and metabolism. These include isoflavones and lignins. Isoflavones are found most commonly in soy products, but also include legumes, alfalfa, clover, licorice root, and kudzu root, and include genistein, daidzein, equol and puerarin. Lignins are an insoluble dietary fiber found in flaxseeds, whole grains, beans and seeds.

• Ensure adequate intake of magnesium and vitamin E.

•Other beneficial micro and phyto-nutrients that impact estrogen metabolism include calcium D-glucarate, curcumin, green tea polyphenols and D-limonene.

Approved By:

Name of Laboratory Director	Laboratory Director
Nutrigenomics Test Lab	CLIA: 123456789

NOTES FOR PRACTITIONERS

***Disclaimer**: These tests were developed and characterized by this laboratory. They have not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.*

Only a qualified healthcare professional should advise a person on the use of information in this report.

All clinical decisions relative to test results should be directed by your qualified healthcare provider. The laboratory makes no representations or recommendations in regards to results.

***Methodology**: All SNP genotyping tests performed using Agena Bioscience MassARRAY technology. All PCR based methods are subject to rare interference such as inhibitors or quality or quantity of DNA. If present, the interference typically yields a no result requiring a repeat rather than an inaccurate one.*

Array based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

***Limitations**: This test will not detect all the known mutations that result in altered or inactive tested genes. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a person has intermediate or high sensitivity phenotypes due to the presence of an undetected polymorphism.*

***HIPAA**: TEST REPORT CONFIDENTIALITY NOTICE: This clinical test report is confidential and intended solely for the use of the individual or entity to whom they are addressed. This report contains confidential information and is intended only for the individual named and his/hers attending qualified healthcare professional. If you are not the intended recipient, you are hereby notified that disclosing, copying, distributing or taking any action in reliance on the contents of this information is strictly prohibited (Federal Regulation 42 CFR, Part 2, and 45 CFR, Part 160).*

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