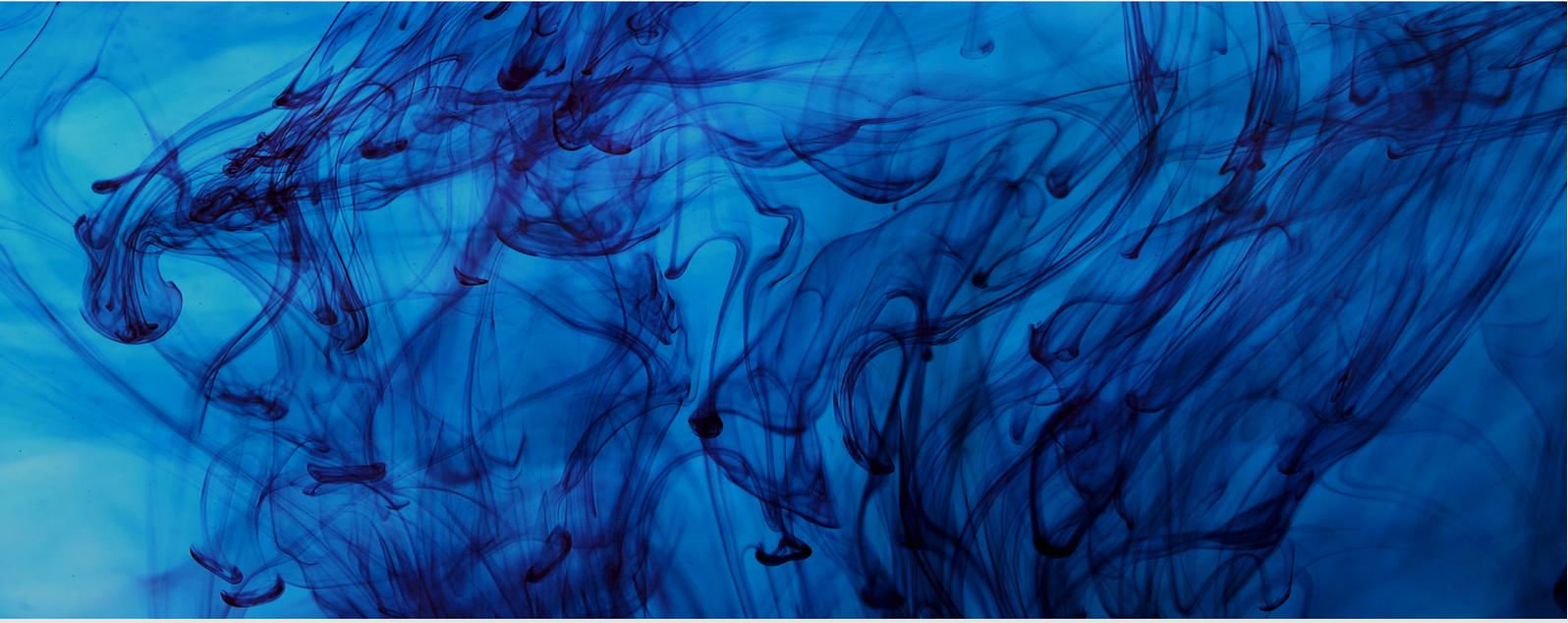




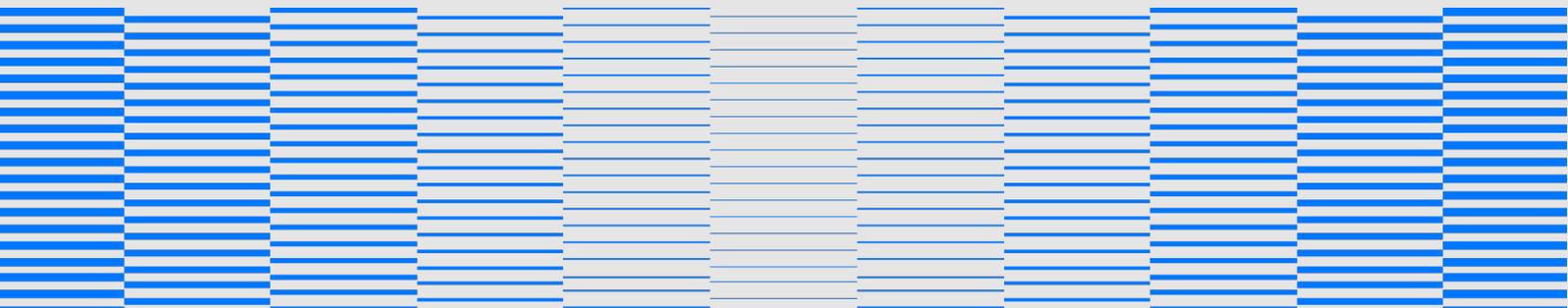
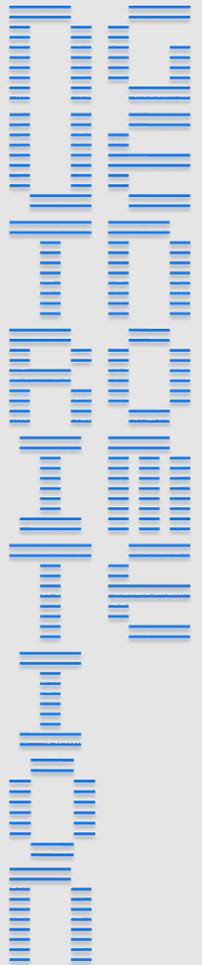
# GENETIC HEALTH ANALYSIS



Welcome to the future of health and human potential

NAME:

DATE: FEB 19, 2022





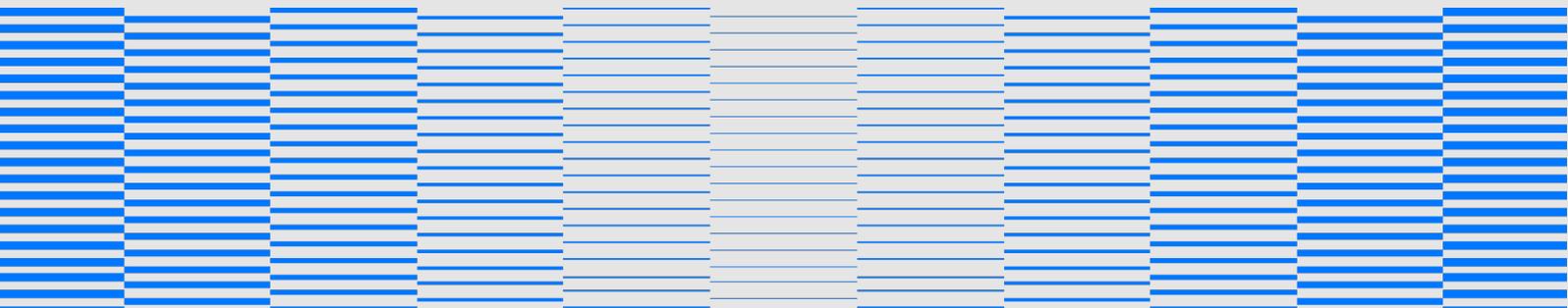
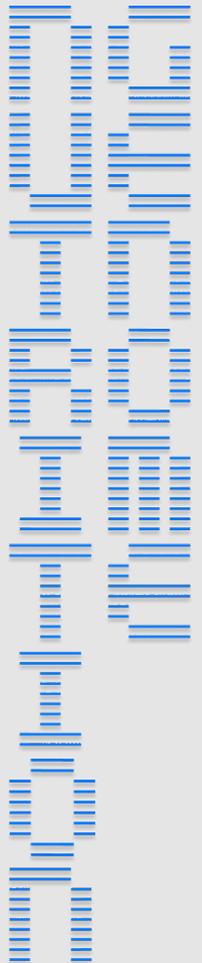
# GENETIC HEALTH ANALYSIS



Nutrition Genome's lab partner is CLIA certified and CAP accredited and performs data analysis on each sample processed to ensure that the sample meets the company's minimum QC threshold for SNPs analyzed.

However, clinical validation of your Nutrition Genome test results have not been established. As such, all information provided is intended for informational, educational, and entertainment purposes only. It is not intended to provide medical advice, to be relied on for medical diagnosis, treatment, or other clinical decision-making, to assess your probability of developing a disease, or to provide you with a genetic carrier risk profile.

Please share your analysis with your doctor if you have any concerns regarding your results or would like to pursue follow up clinical testing under the care of your physician.



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# MACRONUTRIENT METABOLISM

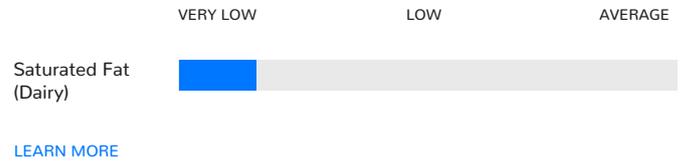
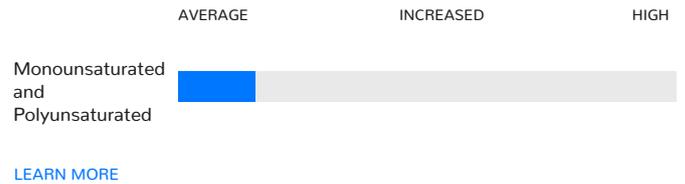
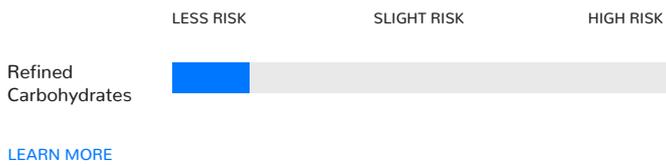
## PROTEIN REQUIREMENTS



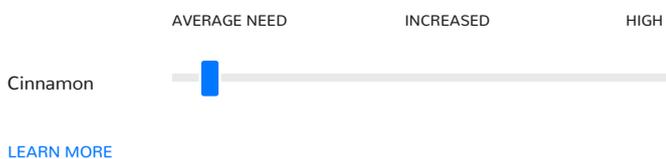
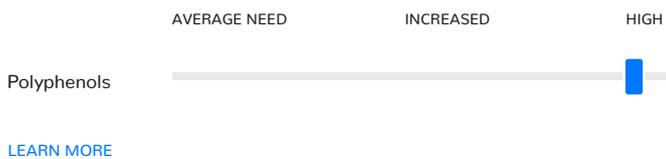
## FAT REQUIREMENTS



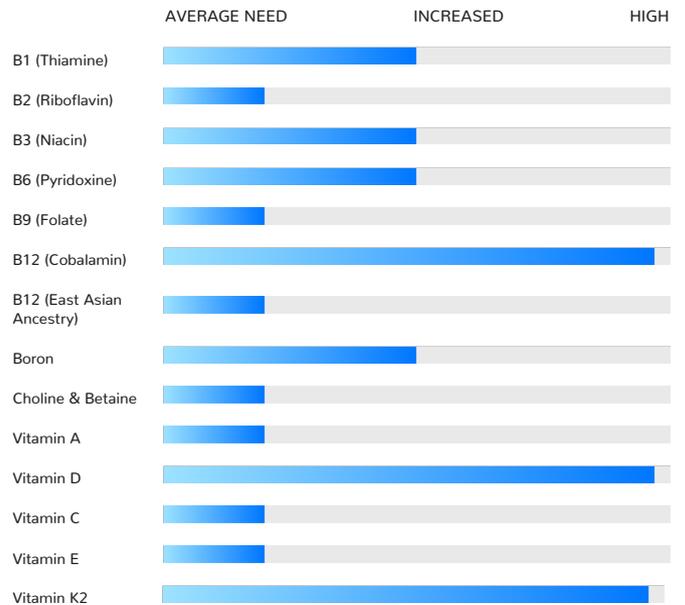
## CARBOHYDRATE REQUIREMENTS



## PHYTONUTRIENT REQUIREMENTS



## MICRONUTRIENT REQUIREMENTS



Cruciferous Vegetables

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AVERAGE NEED      INCREASED      HIGH

Lycopene

[LEARN MORE](#)

AVERAGE NEED      INCREASED      HIGH

Apigenin (Females)

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AVERAGE NEED      INCREASED      HIGH

Apigenin (Males)

[LEARN MORE](#)

AVERAGE NEED      INCREASED      HIGH

Resveratrol

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Magnesium

Manganese

Lithium

Potassium

## CAFFEINE METABOLISM

SLOW

INTERMEDIATE

FAST

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## FIBER REQUIREMENTS

Eat Less

Eat More

AVERAGE NEED      INCREASED      HIGH

Prebiotic Fiber

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## LACTOSE TOLERANCE

TOLERANT

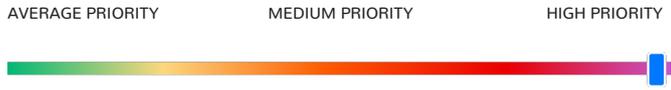
INTOLERANT

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## TOXIN SENSITIVITY

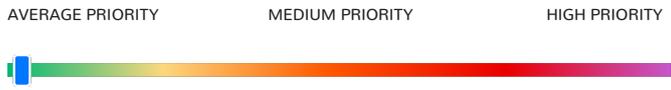
Mycotoxins

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Xenoestrogens

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Ethanol

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Benzo(a)pyrene

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Aromatic Amines

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Aspartame

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Aspartame (East Asian Ancestry)

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Food Dyes

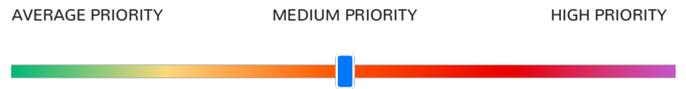
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## PESTICIDES, HERBICIDES AND HEAVY METAL SENSITIVITY

Glyphosate

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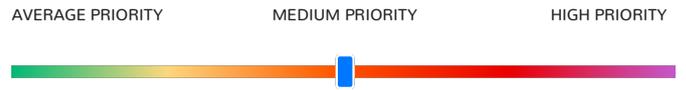
Organochlorines

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Organophosphate Insecticides

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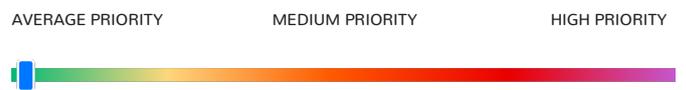
Arsenic

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Cadmium

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Mercury

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# MENTAL HEALTH & COGNITIVE PERFORMANCE

## MENTAL HEALTH AND COGNITIVE PERFORMANCE



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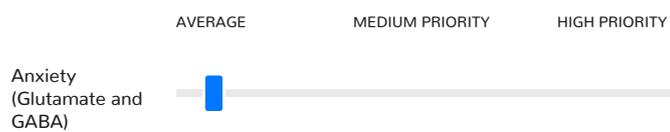
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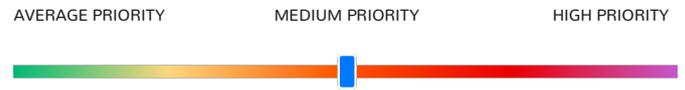


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## STRESS MANAGEMENT

Stress Perception

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Stress and Digestion

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Weight Training and Stress Relief

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## WARRIOR OR STRATEGIST (COMT)

WARRIOR      HYBRID (BOTH)      STRATEGIST



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## SLEEP SUPPORT

LESS LIKELY      AVERAGE      MORE LIKELY



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AVERAGE PRIORITY      MEDIUM PRIORITY      HIGH PRIORITY



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## COVID-19

Glutathione

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Vitamin A

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Vitamin C

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Vitamin D

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B12

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B12 (East Asian Ancestry)

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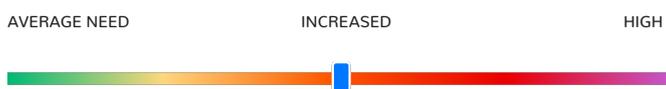
Folate

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B6 (Pyridoxine)

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## BACTERIA, YEAST, PARASITES AND VIRUSES



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### Bifidobacteria

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AVERAGE NEED

INCREASED

HIGH



### Bifidobacteria (East Asian Ancestry)

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AVERAGE NEED

INCREASED

HIGH



### Glycine

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AVERAGE NEED

INCREASED

HIGH



AVERAGE PROTECTION

MODERATE PROTECTION

HIGH PROTECTION

DNA Viruses



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## CARDIOVASCULAR HEALTH

VLDL

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Triglycerides

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ApoB

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Lp(a)

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Raw Plant Intake

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Nitric Oxide

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Homocysteine

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High Blood Pressure

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Blood Clots

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## EXERCISE



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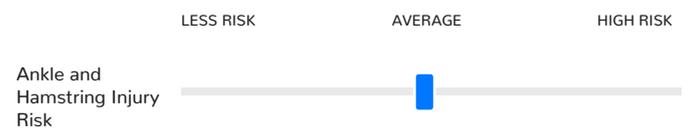
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AVERAGE                      MEDIUM PRIORITY                      HIGH PRIORITY



Uric Acid

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AVERAGE                      MEDIUM PRIORITY                      HIGH PRIORITY



Fibrinogen

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AVERAGE                      MEDIUM PRIORITY                      HIGH PRIORITY



Hemochromatosis

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LESS LIKELY                      SLIGHT RISK                      MORE LIKELY



Caffeine Response for Exercise Under 1 Hour



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LOW                      NO RESPONSE                      HIGH

Caffeine Response for Exercise Over 1 Hour



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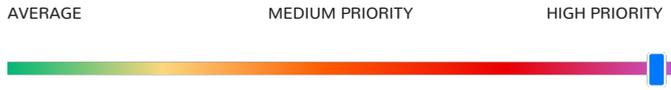


# DNA PROTECTION & REPAIR

## DNA PROTECTION & REPAIR

### Glutathione Protection

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### Mitochondrial Protection

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### UV Protection

[LEARN MORE](#)



### Lung Protection

[LEARN MORE](#)



### Lung Protection (Asian Ancestry)

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### Colon Protection

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### Cured Meat and Colon Health

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### Pancreas Protection

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### Bladder Protection

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AVERAGE

MEDIUM PRIORITY

HIGH PRIORITY



## METHYLATION



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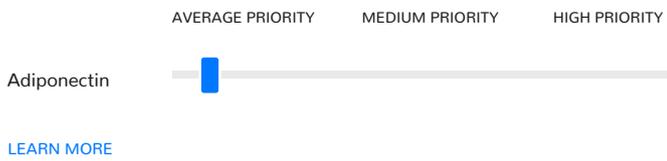
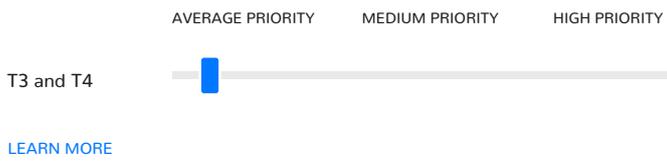
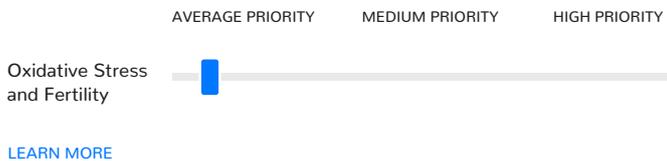
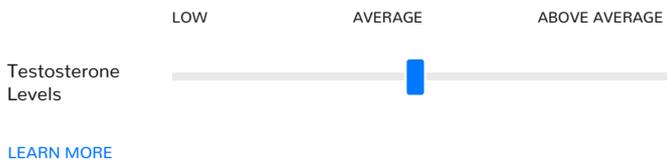
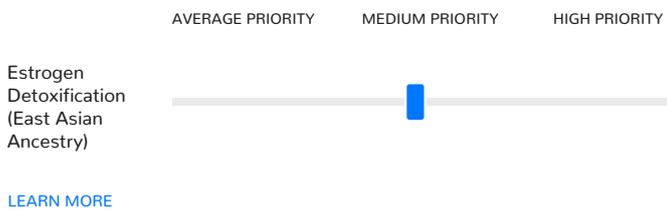
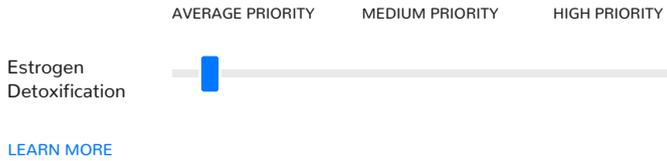


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## HORMONE SUPPORT



AVERAGE PRIORITY    MEDIUM PRIORITY    HIGH PRIORITY

Ghrelin



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# PERSONALIZED BLOOD WORK

These results are generated based on a combination of gene variants unique to you. These biomarkers may not be out of range based on your diet and lifestyle habits, but they may be the ones for you to monitor to ensure you are making the right choices based on your genetic results (your predispositions).

For example, if vitamin D comes up in this section, it does not mean that your current levels of vitamin D are actually low. What we are saying is that based on a variety of genetic factors, your variants could make it more difficult to obtain recommended levels of circulating vitamin D, so it might be prudent to further monitor to ensure that you are taking the necessary steps to turn genetic weaknesses into strengths and maintain correct levels.



**Triglycerides**

Triglycerides should be <150



**B6**

B6 levels may need to be tested



**Fasting Glucose and HbA1C**

Check both fasting glucose and HbA1C



**B12**

If poor B12 status is suspected, methylmalonic acid (MMA) levels may be needed to accurately assess B12 status, absorption, and requirements



**Vitamin D**

Vitamin D should be between 35-50 ng/ml. Check both 25 and 1,25-dihydroxyvitamin D.



## HORMONE SUPPORT

### Vitamin D-CYP2R1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP2R1 rs10741657	Homozygous GG

### Recap



Improves CYP2R1 Gene Function: Sun exposure, adequate vitamin D intake and vitamin D co-factors.



Decreases CYP2R1 Gene Function: Lack of sun exposure, high fructose intake and lack of vitamin D co-factors.

### VITAMIN D-CYP2R1

**Research:** Studies confirm that CYP2R1 is the principal 25-hydroxylase in humans and demonstrates that CYP2R1 alleles have dosage-dependent effects on vitamin D homeostasis.

A 2018 meta-analysis of sixteen articles with a total of 52,417 participants was reviewed for rs10741657. The GG genotype was associated with a clear descending trend of 25(OH)D levels when compared with the AA genotype in Caucasian and Asian populations.

Research has shown that oral administration of vitamin D led to negligible increases in serum 25-hydroxy-vitamin D for homozygotes, and significantly lower increases in serum 25-hydroxy-vitamin D in heterozygous subjects than in control subjects. The heterozygous effect may only be relevant in Caucasian populations.

Vitamin D can influence the expression of more than 1,000 genes and vitamin D deficiency has been linked to fatty liver, seizures, infertility, osteoporosis, cancer, autism (mother deficient), depression, heart attacks, Alzheimer's, dementia, high blood pressure, low testosterone in men, autoimmune disorders and more.

The literature is mixed on optimal vitamin D levels, which most likely vary based on your heritage, skin color and current health issues. The most well documented cause of Vitamin D deficiency is inadequate sunlight exposure such as high latitude countries. Paradoxically, despite its high sunlight hours, vitamin D deficiency is well recognized in Middle Eastern women, inner city young adults in America, athletes and dancers in Israel, elite gymnasts in Australia, young Hawaiian surfers, and adolescent girls in England.

For athletes, vitamin D deficiency has long been associated with muscle weakness and suboptimal muscle function. A positive relationship between serum vitamin D level and jump height, jump velocity and power was found in young women.

Clinical vitamin D deficiency is below 20 ng/ml. There is little evidence to prove there is a benefit for levels above 50 ng/ml. The latest cancer research has found that women with 25(OH)D concentrations greater than 40 ng/ml had a 67% lower risk of cancer than women with concentrations less than 20 ng/ml. Pesticides have been linked to suppressing vitamin D levels and creating a vitamin D deficiency. Your PON1 gene function should also be assessed.

Research has found that sunlight is the optimal way to optimize vitamin D levels along with exercise, vitamin D rich foods and vitamin D cofactors, however supplementation may be necessary.

## Estrogen Metabolism-CYP1A1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP1A1 rs1048943	Heterozygous TC

### Recap



Improves CYP1A1 Gene Function: Iodine, resveratrol, green tea, and decreasing exposure to polycyclic aromatic hydrocarbons.



Decreases CYP1A1 Gene Function: Polycyclic aromatic hydrocarbons (cigarette smoke, vegetable oils, barbecued meat and high grain consumption), dioxins, β-naphthoflavone, omeprazole and primaquine.

### ESTROGEN METABOLISM-CYP1A1

CYP1A1 is also involved in the metabolism of estrogen and benzopyrene (a polycyclic aromatic hydrocarbon) which disrupts DNA methylation and affects breast cancer growth. Variants in CYP1A1\*2C are connected to lung health in Chinese, and breast and prostate health in Caucasians.

Research has shown that optimal levels of iodine can help modulate the estrogen pathway and help prevent cancerous growth by targeting CYP1A1 and CYP1B1. Iodine deficient breast tissue exhibits early markers of breast cancer, and 30% of iodine stores are in the breast tissue.

Researchers also found that a high heterocyclic aromatic amine intake was significantly associated with an increased risk of prostate cancer among individuals with the NAT2 slow acetylator phenotype, CYP1A1 rs1048943 TC and CC genotype, and CYP1A2 AC and AA genotype.

# MACRONUTRIENT METABOLISM

## ALA to EPA and DHA Conversion-FADS2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
FADS2 rs1535	Homozygous GG
FADS2 rs174575	Heterozygous CG

### Recap

 Improves FADS2 Gene Function: EPA and DHA omega-3 fatty acids.

 Decreases FADS2 Gene Function: Relying on plant-based omega-3 fatty acid ALA for those with the heterozygous or homozygous variant.

## ALA TO EPA AND DHA CONVERSION-FADS2

**Research:** You may have a decreased conversion rate of the plant based omega-3 fatty acid ALA to DHA and should choose DHA sources for sufficient omega-3's.

FADS1 and FADS2 are enzymes that are involved in converting omega-3 and omega-6 fatty acids for brain development and inflammation control. Like the lactase gene, FADS1 is likely to be a critical gene of adaptation. In this case, it was in response to a plant-based diet versus a meat and fish based diet depending on migration routes and food availability.

It has been hypothesized that populations that began to rely more on plant-based diets adapted with the selected allele in FADS2 to synthesize more EPA and DHA from plants. The Inuit populations of Greenland, for example, who rely heavily on seafood with very little plant intake, have a deleted allele showing an opposite adaptation to a diet without plants.

A meta-analysis has found an association between variants in FADS2 in European heritage and a low conversion rate of ALA (plant-based omega-3) to DHA. There is also evidence for gene variants in those with African, Chinese, and Hispanic ancestry having a reduced conversion rate.

Children who had a higher dietary ratio of omega-6 to omega-3 were vulnerable for developing colitis if they also presented specific variants in FADS2.

A higher need of animal-based EPA and DHA may be needed for those with variants in FADS2.

## B6-NBPF3

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
NBPF3 rs4654748	Heterozygous TC

## Recap

 Improves NBPF3 Gene Function: B6

 Decreases NBPF3 Gene Function: Sugar, stress, high intake of alcohol and refined flour based carbohydrates, antibiotics, oral contraceptives, ACE inhibitors, antacids, proton pump inhibitors, Phenytoin, bronchodilators, Digoxin, diuretics, hormone replacement therapy, Estradiol, MAO inhibitors, St. John's Wort and Parnate.

## B6-NBPF3

**Research:** You may require a higher intake of B6. Heterozygotes (TC genotype), have a 1.45 ng/mL lower Vitamin B6 blood concentration than the wild-type genotype.

Vitamin B6 plays a major role in neurotransmitter health. B6 deficiency can manifest as anorexia, irritability, anxiety, depression, muscle pain, bad PMS/low progesterone, nausea, seizures, migraines, dermatitis, age related macular degeneration (with low folate and B12) and lethargy.

Researchers have found an inverse association between ovarian cancer risk and vitamin B6 intake. Subjects with the highest vitamin B6 intake showed a 24 percent decrease in the likelihood of developing ovarian cancer compared to the individuals with the lowest intake.

Women of reproductive age, especially current and former users of oral contraceptives, teenagers, male smokers, non-Hispanic African-American men, and men and women over age 65 are most at risk of B6 deficiency. Data suggests that oral contraceptive users have extremely low plasma PLP levels. Three quarters of the women who reported using oral contraceptives, but not vitamin B6 supplements, were vitamin B6 deficient.

## Protein and Fat-ACAT

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ACAT1-02 rs3741049	Heterozygous AG

## Recap

 Improves ACAT Gene Function: B-vitamins 1-5 and lipoic acid.

 Decreases ACAT Gene Function: Medications that deplete B-vitamins 1-5, excess coffee, flour based foods, excess alcohol and excess sugar.

## PROTEIN AND FAT-ACAT

**Improves ACAT Gene Function:** B-vitamins 1-5 and lipoic acid.

**Decreases Gene Function:** Medications that deplete B-vitamins 1-5, excess coffee, flour based foods, excess alcohol and excess sugar.

**Research:** The ACAT gene converts protein and fat to ATP(energy) in the mitochondria, and plays an important role in cellular cholesterol levels. The heterozygous or homozygous ACAT-02 may cause issues with protein and fat metabolism if B-vitamin deficiency is induced.

This gene requires adequate B-vitamins 1-5 and alpha lipoic acid. If you have habits that deplete B-vitamins (medications, excess coffee, flour based foods, excess alcohol, sugar), more stress may be put on the ACAT enzymes and create poor digestion of fat and protein.

## L-Carnitine

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
SLC22A5	Reduced Gene Class Function

## Recap



Improves SLC22A5 Gene Function: Magnesium, vitamin C, lysine and B-vitamins 1-5.



Decreases SLC22A5 Gene Function: Deficiency of magnesium, vitamin C, lysine and B1-5. Dietary habits (medications, excess coffee, flour based foods, excess alcohol, sugar) and medications that deplete vitamin C, magnesium and B-vitamins 1-5 may cause further issues with fat metabolism.

## L-CARNITINE

**Research:** L-Carnitine is responsible for shuttling fats into your cells, modulating your lipid profile, glucose metabolism (carnitine increases the sensitivity of the cells to insulin), oxidative stress, fat loss and inflammatory responses.

Research has postulated that polymorphisms in SLC22A5 (OCTN2) may result in a shortage of carnitine, affecting fatty acid travel into the mitochondria. If you have numerous homozygous genes in SLC22A5, you may have trouble breaking down fats and could be a source of inflammation.

Lysine plays an essential role in the production of carnitine. MCT oil (coconut oil) does not require acetylcarnitine transferase to cross the inner mitochondrial membrane, and therefore, is a good fat for those with multiple homozygous variants in SLC22A5.

## Fat Metabolism-ACSL1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ACSL1 rs9997745	Wild Type GG

## Recap



Improves ACSL1 Gene Function: Total fat intake under 35%, lower saturated fat intake and increased PUFA intake.



Decreases ACSL1 Gene Function: A saturated fat intake over 35%.

## FAT METABOLISM-ACSL1

**Research:** If you have the GG genotype, it may be beneficial for fat intake to be below 35% of your total calories or have a higher intake of polyunsaturated fat from fish, nuts and seeds if you struggle with weight and high glucose.

The GG genotype had higher fasting glucose and insulin concentrations compared with the minor A allele carriers from saturated fat intake, with the result that the GG genotype were more insulin resistant. Among individuals within the top 50th percentile of PUFA intake, the metabolic syndrome risk associated with GG homozygosity was eliminated.

Foods that are higher on the insulin index include dairy and red meat, and insulin inhibits fat breakdown. Fat should come primarily from nuts, seeds, olive oil, avocados, poultry and fish if there are issues with fasting glucose, insulin or weight.

## Lactose

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
LCT rs4988235	Wild Type GG

## Recap

 Improves LCT Gene Function: Lactase.

 Decreases LCT Gene Function: Unknown.

## LACTOSE

**Research:** You may have a decreased ability to breakdown lactose. Most people are born with the ability to digest lactose, the major carbohydrate in milk.

Approximately 75% of the world's population loses this ability at some point, while others can digest lactose into adulthood. The GG genotype is connected to lactose intolerance.

The arrival of farming in Europe around 8,500 years ago necessitated adaptation to new environments, pathogens, diets and social organizations. One of the best examples of genetic dietary changes to this is the lactase enzyme in northern Europeans that only dates to the last 4,000 years.

The ability to digest lactose is much more common in people of European ancestry than those with African or Asian ancestry. This is because dairy was introduced earlier in Europe, approximately 8,000-10,000 years ago.

The GG genotype decreases the ability to breakdown lactose. Avoid dairy or only choose fermented versions of dairy only like yogurt and kefir, and ghee for cooking.

Since this gene only looks at lactose, sensitivities to dairy can still exist. Many people who have issues with cow dairy can often use goat and sheep dairy without issues.

## Ethanol Metabolism-ALDH2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ALDH2 rs671	Heterozygous AG

## Recap

 Improves ALDH2 Gene Function: Hovenia dulcis (oriental raisin tree), clove extract, cysteine, vitamin C and thiamin (B1).

 Decreases ALDH2 Gene Function: Excess alcohol.

## ETHANOL METABOLISM-ALDH2

**Research:** Alcohol, also known as ethanol, is not considered toxic to the body. However, acetaldehyde oxidized from ethanol is considered toxic, and the levels of acetaldehyde produced from alcohol consumption can occur at different rates based on genetics.

The main gene responsible for the conversion of acetaldehyde to acetate is ALDH2 rs671. Variants in ALDH2 have been found to influence the level and accumulation of acetaldehyde in the body, and appears more responsible for alcohol-related adverse reactions including flushing, palpitation, nausea, headache, drowsiness, breathlessness, and general discomfort. This reaction also lowers the risk of alcohol abuse and alcoholism.

What research has found is that alterations in alcohol metabolism occur primarily in Asians, and are very rare in non-Asian populations. Researchers are still puzzled on what environmental or dietary pressure caused this to occur in a specific population.

One speculation is that a higher concentration of acetaldehyde was advantageous for parasitic infections endemic in East Asia, past or present. A likely hypothesis is that tuberculosis is or was an endemic disease in Korean and possibly Japanese and Chinese populations. Infectious diseases are the most -recognized environmental factors that have shaped the human genome during its evolutionary history, and one study demonstrated that variants in ALDH2 rs671 are also associated with a reduced risk of tuberculosis.

The oldest known fermented alcoholic beverage was found in a 9,000-year-old tomb in China, where archeologists unearthed a recipe with hawthorn fruit, sake rice, barley, and honey. If Asia was one of the original locations of alcohol production, it wouldn't seem that this mutation was in a negative response to alcohol consumption and that it should be avoided. Alternatively, the mutation could have occurred to require less alcohol to produce a higher acetaldehyde effect to protect against parasites. The trade-off being that only very small amounts of alcohol should be consumed, with large amounts being more detrimental.

Variants in ALDH2 also increase the risk of acetaldehyde carcinogenesis with alcohol consumption. Alcohol carcinogenesis mostly affects the oral cavity, pharynx, esophagus, larynx, and colon. The liver and breast tissue are also affected by poor alcohol metabolism. Genetic studies of alcohol-associated cancers (upper aerodigestive tract cancers, hepatocellular carcinoma, breast cancer, colon cancer, and thyroid cancer) have repeatedly implicated risk alleles in alcohol metabolism genes, including ADH1B, ALDH2, and other ADH genes, especially in Asian populations.

*Hovenia dulcis*, known as the oriental raisin tree, is mainly found in East Asia. It has long been used as traditional folk remedies for alcohol intoxication. One study found a significant decrease in inflammatory biomarkers for male Koreans using *hovenia dulcis* after alcohol consumption compared to a control group. However, certain genotypes in the CYP2E1 genes may modify the positive response.

In guinea pigs, those with the highest tissue concentration of vitamin C proved to have significantly decreased residual levels of ethanol and acetaldehyde in the liver and the brain. Other animal studies found that cysteine and thiamine also protected against acetaldehyde toxicity.

# INFLAMMATION & ANTIOXIDANT PROTECTION

## Cell Protection-SOD2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
SOD2 rs4880	Heterozygous AG

## Recap



Improves SOD2 Gene Function: Manganese, boron, vitamin A, C, E, omega-3 fatty acids, CoQ10, lutein, lycopene, milk thistle, cordyceps, holy basil, reishi and cryotherapy.



Decreases SOD2 Gene Function: Glyphosate, fluoridated water, chronic stress, poor sleep, shallow breathing, high iron levels and food dyes.

## CELL PROTECTION-SOD2

**Research:** SOD2 is superoxide dismutase, which protects against the inflammatory superoxide inside the cell for the mitochondria (power house of the cell). SOD2 is manganese dependent, and adequate intake is important. Manganese is crucial for heart health, blood sugar, male fertility, bone health and protecting the brain against glutamate toxicity.

Exercise also helps improve SOD2 activity. Studies show exercise intensity can reduce cardiac arrhythmias and myocardial infarction due to improved SOD2 function.

Glutathione level and activity of antioxidant enzymes (catalase, superoxide dismutase, glutathione peroxidase and glutathione reductase) have been found to be increased in yoga practitioners. One year of Tai Chi training has been reported to promote superoxide dismutase activity and lessen lipid peroxidation.

One study found that young men exposed to cryotherapy for 3 minutes at -202°F (-130°C) everyday for 20 days doubled the activity of one the antioxidant enzyme glutathione reductase, and increased superoxide dismutase by 43%.

Chronic stress, poor sleep, shallow breathing and food dye consumption are examples of ways intracellular inflammation can occur. Food dyes have been found to inhibit mitochondrial respiration; the ability of the powerhouse of your cells to convert nutrients to energy and food dyes are often used ironically in sports drinks and multivitamins.

Fluoride decreases SOD2 activity in studies, and 75% of the water in the U.S. is fluoridated compared to 3% of western Europe. Reverse osmosis systems remove fluoride from water.

Variants in SOD2 increase the need for manganese to protect the mitochondria and lactobacillus in the gut. Colitis has been linked to impaired SOD2 genes.

Vitamin, A, C, E, omega-3 fatty acids, cordyceps and reishi help protect mitochondria against intracellular superoxide in red blood cells.

## Glutathione-GSTM1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
GSTM1 rs366631	Wild Type AA

## Recap



Improves GSTM1 Gene Function: Cruciferous vegetables, vitamin C, vitamin A, vitamin E, milk thistle, resveratrol, curcumin, green tea and white tea.



Decreases GSTM1 Gene Function: Low intake of vitamin A, C, E and cruciferous vegetables, smoking, burning of wood or trash, asphalt, coal, diesel exhaust, gas cooking, dioxins, and grilled or charred meat.

## GLUTATHIONE-GSTM1

**Research:** GSTM1 rs366631 is a pseudo-SNP that can be used as a GSTM1 deletion marker. The deletion is also known as the null genotype and confers the absence of the GSTM1 protein. The frequency of the null genotype varies from 20% to 80%, depending on the ethnic group studied.

For example, the null genotype is less frequent in western and southern African populations, less frequent in South American populations, intermediate in the Japanese, but is higher in Egyptian, European, American, and Asian populations.

High frequencies of the GSTM1 null genotype have been found in patients with lung cancer (East Asians), breast cancer (over 50 age group and in Asians), bladder cancer (with NAT2 slow acetylator), colorectal cancer, skin cancer, gastric cancer (among Asians with H. Pylori), chronic bronchitis, kidney disease progression, acute myeloid leukemia, acute lymphoblastic leukaemia, head and neck cancer (combined with CYP1A1 variant), endometriosis, type 2 diabetes retinopathy, and recurrent pregnancy loss. All have been regarded as environmentally induced and the risk may change with ethnicity.

Of the major glutathione enzymes, GSTM1 appears to be the most effective at neutralizing cytotoxic and genotoxic reactive compounds. However, the research shows that the null genotype of GSTM1 on its own may not be able to determine carcinogen exposure cancer risk. Instead, a combination of genotypes in the other glutathione and antioxidant genes like GSTP1 and NFE2L2, detoxification genes like CYP1A1 and NAT2, and/or compounding epigenetic habits that appear to modify the effect.

GSTM1 catalyzes the detoxification of alkyl and polycyclic aromatic hydrocarbons, intermediate forms of many carcinogens, specifically metabolically generated epoxide intermediates of benzo(a)pyrene. Benzo(a)pyrene is part of a class of chemicals called polycyclic aromatic hydrocarbons. Sources of benzo(a)pyrene include the burning of wood or trash, tobacco smoke, asphalt, coal, diesel exhaust, and grilled or charred meat. There is evidence that it causes skin, lung, and bladder cancer in humans and in animals. Research has also shown that early markers of cardiovascular disease are associated with occupational exposure to polycyclic aromatic hydrocarbons.

A study also found sensitivity to gas cooking and the GSTM1 null genotype, increasing the sensitivity of the lungs to nitrogen dioxide. Nitrogen dioxide is also found in diesel exhaust. Exposure of human blood plasma to nitrogen dioxide caused rapid losses of ascorbic acid, uric acid, protein thiol groups, lipid peroxidation, and depletions of alpha-tocopherol, bilirubin, and ubiquinol leading to high levels of oxidative stress.

Animal studies and in vitro studies have shown that vitamin C, vitamin E, vitamin A, resveratrol, curcumin, green tea, and white tea can inhibit the carcinogenic effect of benzo(a)pyrene and nitrogen dioxide. In the Norwegian Mother and Child Cohort Study 50,651 women, a higher prenatal exposure to dietary benzo(a)pyrene was found to reduce birth weight. However, increasing dietary vitamin C intake during pregnancy helped reduce any adverse effects of benzo(a)pyrene on birth weight.

Isothiocyanates from cruciferous vegetables are known for their anti-cancer activity. They are stored as glucosinolates in cruciferous vegetables and are hydrolyzed by myrosinase (an enzyme found in plants and intestinal microflora) to form isothiocyanates. Isothiocyanates from cruciferous vegetables are substrates and inducers of GSTM1.

GSTM1 variants may alter isothiocyanates clearance, with the null genotype retaining higher levels of isothiocyanates and therefore the benefits. In numerous studies, the GSTM1 null genotype was the most responsive to cruciferous vegetables for anti-cancer effects against lung cancer, colon cancer, breast cancer, and kidney disease.

The isothiocyanate levels in cruciferous vegetables will range based on growing conditions including sulfur and nitrogen levels, time after harvest and storage (cold transportation and storage of broccoli also cause a loss of glucosinolates up to 70-80%), plant genetics, and cooking preparation. Broccoli sprouts will yield the highest isothiocyanate levels.

## Glutathione-GSTP1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
GSTP1 I105V rs1695	Heterozygous AG

## Recap



Improves GSTP1 Gene Function: Glycine, cysteine, selenium, vitamin C, B1, B6, zinc, magnesium, optimal iron levels, magnesium, alpha lipoic acid, milk thistle, holy basil and vitamin E supplementation for the homozygous GG genotype only.



Decreases GSTP1 Gene Function: Mercury, arsenic, cadmium, pesticides, and air pollution.

## GLUTATHIONE-GSTP1

**Research:** Glutathione is the master antioxidant system involved in oxidative stress, detoxification and immunity. It requires the amino acids glycine, cysteine and glutamate. Selenium activates the glutathione system and works in concert with vitamin E as a potent antioxidant against plasma and LDL lipid peroxidation.

The functional polymorphism of the GSTP1 Ile105Val gene, which reduces enzymatic activity, involves an A-G substitution. Carriers of these mutations are less able to detoxify carcinogens, and epidemiological studies have suggested that individuals differing in the expression of allelic variants of GSTP1 gene differ in susceptibility to various chemical carcinogens.

A meta-analysis of 10,067 cancer cases and 12,276 controls in 41 independent case-control studies from 19 articles found a significant increase in risk in breast cancer in Caucasians with variants in GSTP1 rs1695. A second meta-analysis found the same results with Asians that had the GG genotype. A 2020 study found that the rs1695 homozygous GG genotype was associated with an increased risk of breast cancer, but not the AG genotype. Other research has shown the risk to be higher in premenopausal women vs. post-menopausal women.

An analysis of that included 3,035 breast cancer cases and 3,037 population controls in a Chinese population found that cruciferous vegetable intake helped offset the risk of the GG genotype, with a lower risk associated with a higher cruciferous vegetable intake.

A meta-analysis of 11,762 cases and 15,150 controls from 51 studies showed a statistically significant association between GSTP1 rs1695 polymorphism with prostate cancer risk and urinary system cancer among Asians.

GSTP1 rs1695 variants were reported to be associated with the risk of esophageal cancer and malignant melanoma in the Caucasian population, but not childhood acute lymphoblastic leukemia or bladder cancer.

Glutathione-related polymorphisms, such as GSTM1 and GSTP1 have also been found to increase the elevation and toxicity of mercury. Selenium blocks mercury uptake, folate decreases mercury levels and magnesium and holy basil protect against mercury toxicity.

One benefit of the GSTP1 AG and GG genotype appears to be in athletic training. GSTP1 rs1695 AG and GG may be high responders to endurance training due to an impaired ability to remove excess reactive oxygen species. The hypothesis is that better activation of cell signaling pathways results in positive muscle adaptations. Women with at least one copy of the G allele showed a significantly greater increase in V·O<sub>2</sub>max in response to applied training.

In healthy control subjects, the effect of α-tocopherol supplementation on the production of inflammatory cytokines appears to be dependent on an individual's GSTP1 rs1695 genotype. These genotype-specific differences may help explain some of the discordant results in studies that used vitamin E. Persons having the alleles AA or AG in GSTP1 rs1695 had an increase in inflammatory interleukin-6 (IL-6) upon supplementing alpha-tocopherol (the most common form of Vitamin E in a North American diet) while those with GG saw a decrease.

## Nitric Oxide-NOS1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
NOS1 rs2293054	Homozygous AA

## Recap



Improves NOS1 Gene Function: Carotenoids, polyphenols and DHA.



Decreases NOS1 Gene Function: Psychological stress and pesticides.

## NITRIC OXIDE-NOS1

**Research:** Nitric oxide acts as a neurotransmitter, neuromodulator, vasodilator, anti-microbial, ant-tumorigenic, insulin secretions, peristalsis, inhibiting calcium entry into the cell, increasing potassium channels, and decreasing intracellular calcium.

NOS1 has a role in the regulation of the serotonin pathway, the HPA axis, and psychological stress. Chronic stress increases NOS1 expression in many parts of the brain, including the hippocampus (affecting emotion and memory). Recent studies have reported gene-specific and global changes in DNA methylation in response to psychological stress in humans. Chronic psychosocial stress has been associated with accelerated aging at the cellular level including shortened telomeres, low telomerase activity, decreased antioxidant capacity, and increased oxidative stress.

Variants in NOS1 may benefit from balancing the HPA axis (primary stress response system) and polyphenol consumption. There is considerable evidence showing that cellular oxidative damage occurring in Parkinson's disease might result also from the actions of altered production of nitric oxide. Polyphenols modulate neuroinflammation by inhibiting the expression of inflammatory genes and the level of intracellular antioxidants.

NOS1 also plays a role in oxidative stress and cancer prevention. For oxidative stress, interactions were found between pesticides, SOD3, and the NOS1 SNPs rs12829185, rs1047735, and rs2682826. The foods correlated in research to improved NOS1 function include carrots, tomatoes, squash, corn, orange peppers, red peppers, yellow peppers, pumpkin, red beets, red onions, yellow beets, and sweet potatoes to offset oxidative stress. One study found that carriers of the variant allele for NOS1 (rs2293054) that had the highest intake of these foods had a 50% reduced risk of non-Hodgkin's Lymphoma and up to 30-70% reduced risk of diffuse large B-cell lymphoma.

## Nitric Oxide-NOS2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
NOS2 rs2248814	Homozygous AA

## Recap



Improves NOS2 Gene Function: Eggs, coconut, walnuts, almonds, sunflower seeds, pumpkin seeds, sesame seeds, seaweed, whey protein, cordyceps mushrooms.



Decreases NOS2 Gene Function: Smoking, heavy metals, vegetable oils, high blood sugar, high acidity and poor breathing habits.

## NITRIC OXIDE-NOS2

**Research:** NOS2A encodes for wound, tissue damage, infection and hypoxia (low oxygen).

NOS2A or iNOS normally induces low amounts of nitric oxide, but under pathogenic conditions, high levels of nitric oxide are generated to combat environmental insults in a wide range of cells.

Nitric oxide uncoupling occurs due to chronic stress, poor diet and environmental stressors including heavy metals, vegetable

oils, high blood sugar, high acidity and poor breathing habits.

Research has found that significant interaction between smoking and the NOS2A SNP rs2248814. Stratified data by genotypes demonstrated that the association between age-related macular degeneration (AMD) and smoking was stronger in carriers of AA genotypes than in carriers of the AG genotype or GG genotype. AA homozygous individuals with AMD were 35 times as likely to have smoked as controls with the AA genotype.

For eye health, please review the CFH and ARMS2 gene in conjunction with NOS2A for dietary strategies.

The rs2248814 NOS2A may also have a compounding effect for delayed fracture healing. The AA genotype of NOS2A could benefit from whey protein to normalize NOS levels, lower oxidative stress and increase wound healing. Whey protein was found to significantly decrease the levels of nitric oxide (NO) and decrease the time required for wound healing. In mice studies, whey protein has also been found to improve fracture healing.

### Eye Health-ARMS2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ARMS2 rs10490924	Homozygous TT

### Recap



Improves ARMS2 Gene Function: Lutein, zeaxanthin, bilberry, lingonberry, vitamin C, vitamin E, DHA, and zinc.



Decreases ARMS2 Gene Function: Smoking, pesticides, benzene (found in certain laundry detergents, gasoline and paint), aspartame, oxidative stress, elevated TNF-alpha, elevated IL-6, obesity, smoking, diabetes, hypertension, atherosclerosis and low intake of lutein and zeaxanthin.

### EYE HEALTH-ARMS2

**Research:** ARMS2 is considered a second major AMD susceptibility gene next to CFH. CFH and ARMS2 share a common pathway in the pathogenesis of AMD, with ARMS2 polymorphisms disrupting mitochondrial function in the retina.

Research estimates that the risk of AMD can be attributed to 20% from smoking, 36% for variants in ARMS2, and 43% for variants in the CFH gene.

The overall effect of ARMS2 polymorphisms is driven primarily by a strong association in smokers. This gene-environment interaction is supported by statistically independent family-based and case-control analysis methods. Studies have shown that a genetic susceptibility coupled with a modifiable lifestyle factor such as cigarette smoking confers a significantly higher risk of AMD than either factor alone.

Polymorphisms in ARMS2 is also associated with polypoidal choroidal vasculopathy (PCV) and clinical severity in the subgroups of PCV in the Japanese population.

# MENTAL HEALTH & COGNITIVE PERFORMANCE

## MAO-Serotonin

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
MAO-A rs6323	Homozygous GG

## Recap



Improves MAO-A Gene Function: Vitamin B6, folate, B12, B2, magnesium, vitamin C and probiotics.



Decreases Gene Function: Antibiotics, aspartame, oral contraceptives, proton pump inhibitors, high estrogen levels, constipation and deficiencies in the vitamins and minerals above.

## MAO-SEROTONIN

**Research:** MAO-A (Monoamine oxidase A) is a critical enzyme involved in breaking down important neurotransmitters such as serotonin, estrogen, norepinephrine, and dopamine.

You have the GG genotype that encodes for the high activity version of the enzyme. While the GG genotype has produced mixed results with depression, low estrogen in women combined with the GG genotype may lead to depression from low serotonin, poor sleep from low melatonin and sugar/refined carbohydrate cravings and increased alcohol consumption (the body's way to temporarily boost serotonin but with bigger drops). The artificial sweetener aspartame inhibits the carbohydrate-induced production of serotonin, creating higher cravings. When serotonin levels are optimal, sugar and carbohydrate cravings go down.

Curcumin has antidepressant activity, potentially through inhibiting MAO and increasing the concentration of serotonin, dopamine and epinephrine in the synapse and thus prolonging their action (similar mechanism to SSRI drugs). By modulating MAO and COMT (optimal magnesium, vitamin C and copper levels) together, normal levels of these neurotransmitters can be achieved. Avoid aspartame, which may lower serotonin levels further.

Serotonin levels are more complicated than assessing just MAO-A, including estrogen fluctuations, chronic stress, antibiotic use and general gut health, COMT function, and serotonin transportation and receptor genes. Serotonin is responsible for well-being, happiness, memory and appetite. When serotonin is too low, it can cause depression, lack of ambition, and a struggle to derive pleasure from life. When it is dysregulated, it can cause IBS, mania, OCD, and drug-induced serotonin syndrome.

To modulate healthy serotonin levels, research has found that aerobic exercise to fatigue, strength training, yoga and nature walks all are effective. Fermented foods and probiotics (90% of serotonin is made in the gut), getting more sunlight or taking vitamin D, dark chocolate, fish oil, and a weekly massage are also excellent strategies. However, both extremes of a sedentary lifestyle and excessive exercise negatively affect MAO-A.

## Serotonin Receptor-Stress

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
5-HT2A rs6313	Heterozygous AG
5-HT2A rs6311	Heterozygous TC

## Recap



Improves Gene Function: Moderate intensity aerobic exercise, cognitive behavioral therapy, mindfulness training, meditation, yoga, tryptophan, green or black tea, prebiotics, probiotics, B2, B6, B12, and folate.



Decreases 5-HT2A Gene Function: Chronic stress, poor gut flora, high-dose lithium, cannabis abuse, and excessive smartphone use.

## SEROTONIN RECEPTOR-STRESS

**Research:** The serotonin 2A receptor (5-HT2A) has been implicated in mental disorders with complex etiologies that are still not clearly understood, in processes such as learning and memory, and also in neurogenesis. Although the functional significance of 5-HT2A polymorphisms are not entirely understood, there is evidence that rs6311 modulates transcription factor binding and promoter methylation, affecting gene transcription (the first step of gene expression).

The T allele of the 5-HT2A gene rs6311 has been shown to increase the 5-HT2A expression in vitro and is associated with anxiety, IBS and depressive disorders. It has also been hypothesized that 5-HT2A variants may influence resting vagal activity among persons with chronically high levels of perceived stress.

One meta-analysis showed that the T allele of rs6311 or the linked A allele of rs6313 was significantly associated with obsessive compulsive disorder (OCD). This result was confirmed in the author's subsequent comprehensive meta-analysis in 2016 with a larger dataset. Multiple studies in this analysis indicated that the rs6311 T allele was more abundant in females with OCD compared to control females.

Another meta-analysis of 37 twin samples suggests that obsessions and compulsions arise from a combination of genetic factors and non-shared environment. OCD might be shaped by a large number of genes of modest impact, which combine to influence the risk for developing OCD. Polymorphisms in genes related to BDNF, GABA, glutamate, serotonin, acetylcholine, glycine, ubiquitin, bradykinin, myelinization, TNFA, gender and environmental trauma may all have a cumulative effect on whether or not someone develops OCD.

Psoriasis is a chronic inflammatory skin disease affecting about 2-4% of the population worldwide, and is thought to be a multifactorial disease with both genetic and immunogenic backgrounds. Psoriasis occurs in connection with stress and mood disorders and is apparently induced in patients who have been treated with antidepressants. The serotonergic system, which consists of serotonin-producing cells, serotonin receptors and serotonin transporters, may play a significant role in psoriasis.

Theanine, a component of green tea and black tea, has been shown to increase BDNF levels, modulate serotonin and dopamine levels, and improve learning and memory. It has shown promise as an adjunct therapy for schizophrenia and depression, and researchers believe there may also be an application for anxiety disorders, panic disorder, OCD, and bipolar disorder.

Vagus nerve stimulation may be a promising add-on treatment for anxiety, depression, PTSD, seizures, and inflammatory bowel disease. Natural ways to stimulate the vagus nerve and increase vagal tone include singing, deep breathing, meditation and yoga. Another way is to make a dietary shift towards good gut bacteria, shown to influence the activity of the vagus nerve.

In human volunteers as well as in a rat model, administration of a probiotic formulation consisting of *Lactobacillus helveticus* R0052 (traditionally used in the manufacture of Swiss-type cheeses and long-ripened Italian cheeses such as Emmental, Gruyere, Grana Padano and Parmigiano Reggiano) and *Bifidobacterium longum* R0175A (colonizes at birth, but levels vary genetically) significantly attenuated psychological distress and reduced anxiety-like behavior. Research has also found that prebiotics can improve non-REM sleep as well as REM sleep after a stressful event.

One pilot study found that a 12-week moderate intensity aerobic exercise program reduced OCD symptoms and the reductions lasted 6 months later.

tremendous results, exceeding effects typically observed with individual and group-based cognitive behavioral therapy for OCD based on leading meta-analytic reviews.

## Dopamine, Adrenaline and Estrogen-COMT

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
COMT rs4633	Wild Type CC
COMT V158M rs4680	Wild Type GG

### Recap

 Improves COMT Gene Function: Vitamin C, magnesium, and copper (copper should not be too low or too high).

 Decreases Gene Function: Chronic stress, sugar, proton pump inhibitors, aspartame, low magnesium levels, low vitamin C levels, low and high copper levels, constipation, xenoestrogens, high homocysteine levels, high SAH levels, estrogen-based medications and mercury toxicity.

## DOPAMINE, ADRENALINE AND ESTROGEN-COMT

**Research:** COMT (catecholamine methyltransferase) shares a pathway with MAO-A and is the gene for dopamine, estrogen, adrenaline and catecholamine metabolism. This pathway requires magnesium, vitamin C and copper as co-factors.

While the homozygous genotype for COMT V158M is associated with slower enzymatic function and naturally higher dopamine and adrenaline levels, the wild-type COMT V158M gene (GG rs4633) is associated with faster enzymatic function, leading to lower prefrontal dopamine, adrenaline and norepinephrine levels.

The benefits to the GG genotype may be a better response to high-pressure situations and the ability to be more emotionally resilient and calm in a crisis. Those with the GG genotype may even thrive more in response to certain stressors and have enhanced cognitive performance due to the elevation of dopamine and adrenaline to more normal levels.

The downside of the GG genotype is that it can affect executive function and problem-solving abilities compared to the AC and AA genotypes of COMT V158M if dopamine remains low. Individuals who had the GG genotype of COMT and variants in ANKK1 showed the lowest cognitive performance, however, both genes can be improved by increasing catecholamine intake, meditation, balanced blood sugar, vitamin D, omega-3 fatty acids, fiber, high intensity exercise and lower media exposure.

Several studies have found that the COMT V158M GG individuals perform better than those with the AA allele on tasks demanding cognitive flexibility, while individuals with the AA allele are better at tasks demanding focused attention. The “inverted U” hypothesis suggests that when dopamine levels are either too high or too low, cognition is adversely affected.

In a study of Swedish men and women with depression, the GG genotype also appears deleterious with a three-fold increased risk of later cardiovascular disease compared to those non-depressed carrying the GG genotype. The risk was higher in women than in men. A 2016 meta-analysis found that for each cup of coffee, depression was reduced by 8%, being most significant when the caffeine consumption was above 68mg/day and below 509mg/day. Due to coffee and caffeine’s effect on COMT and dopamine, this genotype with depression may benefit from increased coffee intake. The CYP1A2 gene for caffeine metabolism should also be reviewed.

Small studies have shown that Caucasian carriers of at least one G allele showed a greater effect for social facilitation and cooperativeness (working together in a group) than the AA homozygous group for COMT V158M. In women, the GG genotype was considered to be more helpful and empathetic, socially tolerant, compassionate, and potentially more altruistic.

The GG genotype has also been found to have a higher threshold of pain. In a 2019 study, twenty minutes following exposure to cold stress, subjects with the GG genotype showed a lower biochemical stress response relative to the homozygous AA carriers.

While studies have had mixed results with ADHD and COMT genotypes, research has shown that amphetamines (Adderall) enhanced prefrontal cortex function and improved working memory efficiency for the GG (high COMT activity) subjects, while amphetamine produced adverse effects under high working memory load conditions for homozygous AA (low activity) subjects. A subtype of ADHD is characterized by low dopamine levels.

There are dietary strategies that naturally slow down the COMT enzyme. Catecholamines (coffee, black tea, green tea, red wine, chocolate, citrus, bananas, berries, and vanilla) all help slow down COMT, increasing dopamine and adrenaline. For breast cancer prevention, green tea has been found to be beneficial in the AG and AA genotype, but not the GG genotype. This is due to the AG and AA genotype retaining polyphenols the longest. Therefore, the GG genotype may need a higher intake of green tea to achieve the same benefit.

Coffee can increase dopamine concentration, signaling, and receptor availability, proving very beneficial for those in a lower dopamine state. Research has also found that coffee drinkers have up to a 60% lower risk of Parkinson's disease likely due to increased dopamine signaling in the brain from caffeine.

Those with lower dopamine and adrenaline levels are also going to do better with exercise that involves an element of risk like surfing, snowboarding, mountain biking, skiing, and athletic competitions to modulate healthy dopamine and adrenaline concentrations. This requirement may be more relevant in men due to higher estrogen levels in women slowing down COMT.

## Dopamine Receptors-ANKK1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ANKK1 rs1800497	Heterozygous AG

### Recap



Improves ANKK1 Gene Function: Meditation, 8 hours of sleep per night, balanced blood sugar, vitamin D, omega-3 fatty acids, fiber, high intensity exercise and lower media exposure.



Decreases ANKK1 Gene Function: Low blood sugar, refined sugar, high fructose corn syrup, elevated lead levels, elevated copper levels, iron deficiency, omega-3 deficiency, low vitamin D levels and excessive media exposure.

## DOPAMINE RECEPTORS-ANKK1

**Research:** Dopamine is a neurotransmitter with numerous roles, including reward-motivated behavior and social behavior.

Dopamine is involved in trial-and-error learning. Variants in genes related to dopamine signaling may also affect a person's ability to learn.

The heterozygous AG and homozygous AA genotypes have been correlated with up to a 30% reduction in dopamine receptors in a region of the brain known as the striatum. One small study found that people with the wild-type GG genotype learned from their mistakes easily, while people with the AG or AA genotypes were more likely not to learn from their mistakes and repeat behavior with negative consequences.

Those with sugar addictions, compulsive eating and obesity may have systems that need much more stimulation to feel pleasure caused by fewer D2 dopamine receptors and the need for extra stimulation to make the receptors "turn on." Functional MRI studies of teenagers, both lean and obese, found that the teenagers whose brains didn't light up as much in the dopamine reward centers were more likely to be obese and gain weight later. They also were more likely to have fewer dopamine receptors.

Poor dopamine uptake may contribute to the development of obesity. This relationship was significantly stronger in women with a heterozygous or homozygous A1 variant in rs1800497. The "A" corresponds to the A1 allele and the "G" is called the A2 allele. A1 heterozygous or homozygous women had lower dopamine activation in response to food, and therefore gained more weight potentially due to their diminished pleasure response from dopamine.

Fourteen studies investigated mindfulness meditation as the primary intervention and assessed binge eating, emotional eating, and/or weight change. Results suggest that mindfulness meditation effectively decreases binge eating and emotional eating in

populations engaging in this behavior. However, evidence for its effect on weight is mixed.

Researchers found that individuals with Internet addiction showed reduced levels of dopamine D2 receptor availability in subdivisions of the striatum. This helps explain the universal iPhone phenomenon of addictive-reward behavior, with excessive use decreasing dopamine receptors and increasing the craving for more.

The global statistics show that about 10 percent of the world's population has ADHD. When researchers looked specifically at teenagers in the US, they found the diagnoses had risen 52 percent since 2003. ADHD has been associated with decreased dopamine activity. A meta-analysis of 11 studies with 1645 cases and 1641 controls found that variants in rs1800497 may be associated with ADHD.

Studies have also found that children and adults with ADHD are significantly more likely to be overweight, showing the shared connection to decreased dopamine levels. The heavy metal lead disrupts the dopamine pathway, and 16 out of 18 studies found a significant association between blood lead levels and one of the types of ADHD (Combined / Inattentive / Hyperactive-Impulsive). Other research has shown that iron deficiency causes a reduced number of dopamine receptors, and a recent study from the Annals of Medical and Health Sciences Research found that low serum iron, ferritin levels, and vitamin D deficiency may be associated with ADHD.

Vitamin C is proposed as a neuromodulator of glutamate, dopamine, acetylcholine and GABA transmission and related behaviors. One study showed that following a long period of vitamin C deficiency, depressed levels of both dopamine and norepinephrine were reported. Vitamin C also reduces blood lead levels.

Mindfulness training may improve self-regulation of attention. Neuroimaging studies suggest that mindfulness meditation engenders neuroplastic changes in brain areas associated with attentional functioning typically impaired in ADHD. One study found meditation increased endogenous dopamine release of 65% in the ventral striatum during meditation.

## Anandamide-FAAH

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
FAAH rs324420	Wild Type CC

## Recap

 Improves FAAH Gene Function: Exercise over 30 minutes, red clover tea (women), kaempferol, cacao, genistein (fermented soy), Echinacea, 7-hydroxyflavone (parsley, onions, berries, tea, and citrus fruits), l-caryophyllene (cloves, rosemary, hops).

 Decreases FAAH Gene Function: Pesticides and phthalates.

## ANANDAMIDE-FAAH

Anandamide is a neurotransmitter and endogenous cannabinoid, and is known as the "bliss" molecule that targets the endocannabinoid system.

The endocannabinoid system is involved in many physiological processes including reward, addiction, fertility, pain and energy regulation. This system was named from the cannabis plant, such as marijuana and hemp. THC closely resembles anandamide.

The endocannabinoids play a significant role in pain modulation and inflammation, and have been demonstrated to relieve pain by activating the CB1 and CB2 receptors.

The wild-type genotype (CC) encodes for the fast activity of FAAH, and therefore naturally leads to lower anandamide levels. Those with the homozygous genotype (AA), have the slow-activity of FAAH and naturally higher levels of anandamide. This means that the CC individuals may have more anxiety and have to work harder to achieve higher levels of happiness, while the AA individuals have less anxiety and naturally higher levels of the "bliss" molecule that stimulate feelings of happiness.

Low levels of anandamide have been linked to slower extinction of fear memories and a heightened stress response to threatening situations than those with higher anandamide levels. Healthy volunteers who carried the rs324420 "A" allele (low

FAAH activity, high anandamide levels) had much less amygdala activation when placed in a threatening situation. They also had a weaker correlation between amygdala activation and trait anxiety, which is a general tendency to perceive situations to be threatening and to respond to such situations with subjective feelings of apprehension and tension.

Pesticides such as chlorpyrifos and diazinon alter the endocannabinoid system and researchers have hypothesized that eating organic foods lacking pesticide residues may promote endocannabinoid balance. Phthalates are plasticizers added to water bottles, tin cans, food packaging, and even the enteric coating of pharmaceutical pills. Phthalates may act as endocrine disruptors and carcinogens, and have been found to block CB1 receptors, found in the brain.

However, there are also ways for people to lower excessive levels of chronic stress and anxiety by increasing anandamide levels in the body. One of the best ways to do this is with exercise. Endorphins (endogenous opioids) enhance the effects of cannabinoids and what has been known as the "runner's high" may in fact be the increase of anandamide. Research found that running and biking over 30 minutes, along with strenuous hiking at high altitude significantly increased anandamide.

Clinical anecdotes suggest that stress-reduction techniques, such as meditation, yoga, and deep breathing exercises impart mild cannabimimetic effects.

# DETOXIFICATION

## Liver Enzyme-CYP1A1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP1A1*2C 4889 rs1048943	Heterozygous TC

## Recap

 Improves CYP1A1 Gene Function: Iodine, resveratrol, green tea, and decreasing exposure to polycyclic aromatic hydrocarbons.

 Decreases CYP1A1 Gene Function: Polycyclic aromatic hydrocarbons (cigarette smoke, vegetable oils, and high grain consumption), dioxins, β-naphthoflavone, omeprazole and primaquine.

## LIVER ENZYME-CYP1A1

**Research:** CYP1A1 is in the estrogen pathway along with CYP1B1, CYP1A2, CYP3A, SULT's, and COMT. It catalyzes many reactions involved in drug metabolism and estrogen. It is induced by PAH - polycyclic aromatic hydrocarbons - (cigarette smoke, burning coal, vegetable oils, and grains). CYP1A1 is connected to lung health in Chinese, breast and prostate health in Caucasians, and colon health in Asians, Caucasians, and mixed populations.

A combination of the GSTM1 null genotype and variants in CYP1A1 was found in head and neck cancer cases.

Variants in CYP1A1 may make you more sensitive to the harmful effects of benzopyrene found in cigarette smoke. Research has shown that early markers of cardiovascular disease are associated with occupational exposure to polycyclic aromatic hydrocarbons.

Resveratrol is a naturally occurring compound that has been shown in a number of studies to inhibit the induction of CYP1A1 and CYP1B1 by dioxin.

One study detected an inhibitory effect of green tea extract on the carcinogenesis induced by the combination of asbestos and benzopyrene in rats drinking 2% green tea extract throughout their lives.

Due to variants in CYP1A1, you will want to reduce exposure to tobacco smoke, vegetable oils, and charred meat.

## Liver Enzyme-CYP1B1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP1B1*6 L432V rs1056836	Wild Type GG

## Recap



Improves CYP1B1 Gene Function: Iodine, apigenin, quercetin, myricetin, chrysoeriol (rooibos tea and celery) ghee, vitamin C and resveratrol.



Decreases Gene Function: Heterocyclic amines, xenoestrogens, high biotin supplementation, oral contraceptives, hormone replacement therapy, excessive sun exposure, vegetable oils, grains, fried meat, excess of smoked foods, cigarette smoke exposure and exhaust.

### LIVER ENZYME-CYP1B1

**Research:** Due to the carcinogenic activation of polycyclic aromatic hydrocarbons (cigarette smoke, burning coal, vegetable oils, grains) and estrogens to genotoxic catechol estrogens - both which cause DNA mutations - variants in the CYP1B1 gene are important for breast, ovarian, colon, lung and prostate health. This is especially true for those with variants in GSTM1 and GSTP1. CYP1B1 may also be important for skin health, with excessive sun exposure negatively affecting CYP1B1 expression.

CYP1B1 participates in the first step of estrogen metabolism, the conversion of estrogens to 2- or 4-hydroxyestrogens, and specifically catalyzes the 4-hydroxylation of estrogens. 4-hydroxyestradiol is inactivated by COMT.

According to NCBI, C encodes the Leucine and G the Valine. The CYP1B1 L432V rs1056836 GG (valine) is associated with increased CYP1B1 messenger ribonucleic acid (mRNA) expression with a subsequent elevation in 4-hydroxyestradiol formation resulting in increased estrogen-mediated carcinogenicity. However, this has not been proven in human studies.

Minimizing polycyclic aromatic hydrocarbons, xenoestrogens and high estrogen levels in the body are a priority for CYP1B1. Vegetable oils (soy, corn) have been found to be one of the highest sources of polycyclic aromatic hydrocarbons, while also being a high source of omega-6 fatty acids that can disturb the healthy omega-3 and omega-6 ratio needed to prevent skin cancer growth.

A meta-analysis of 12 studies found that coffee consumption decreased the risk of cutaneous melanoma, while another study found that 2 cups of dark roast coffee per day for one month caused a 23% reduction in DNA damage.

Research has shown that optimal levels of iodine can help modulate the estrogen pathway and help prevent cancerous growth by targeting CYP1A1 and CYP1B1. Iodine deficient breast tissue exhibits early markers of breast cancer, and 30% of iodine stores are in the breast tissue.

One study found that high-dose biotin supplementation (often used in isolation for hair growth) increased CYP1B1 expression and was associated with an increase in the occurrence of single-stranded DNA breaks compared with biotin-deficient cells; while inhibitors of CYP1B1 prevented DNA strand breaks.

Inhibition of CYP1B1 activity was observed for the flavonols quercetin, apigenin and myricetin, while resveratrol has shown to convert to piceatannol through CYP1B1, a tyrosine kinase inhibitor and a compound of known anticancer activity. Chrysoeriol, present in rooibos tea and celery, also acts selectively to inhibit CYP1B1 in vitro and may be especially relevant to patients with CYP1B1 overactivity.

One study in 259 post-menopausal women found that for those with certain genotypes in CYP1B1 (rs1056836), KRAS (rs61764370) and MTHFR (rs1801133 and rs1801131), oral contraceptives and hormone replacement therapy was associated with shorter leukocyte telomere length. Shorter leukocyte telomeres are connected to premature aging, and may increase the risk of cancer, cardiovascular disease, obesity, diabetes, chronic pain, and sensitivity to perceived psychological stress.

In observational studies, higher levels of exercise are related to longer telomere lengths in various populations, and athletes tend to have longer telomere lengths than non-athletes. This relationship is particularly evident in older individuals and physical activity may confer protection against stress-related telomere length shortening.

Higher coffee consumption has been associated with longer telomeres among female nurses. Be aware that there is a compounding effect with caffeine on the slow metabolizer CYP1A2 CC genotype. Research has shown that oral contraceptives significantly prolong the half-life of caffeine from 6.2 hours to 10.7 hours, and therefore could theoretically cause more cardiovascular issues from caffeine for the CYP1A2 CC genotype.

### Vitamin K2-VOKRC1\*2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
VKORC1*2 rs9923231	Homozygous TT

## Recap



Improves VOKRC1\*2 Gene Function: Vitamin K2, probiotics and prebiotics.



Decreases Gene Function: Warfarin, statin drugs, antibiotics and vitamin K2 deficiency.

## VITAMIN K2-VOKRC1\*2

**Research:** Vitamin K2 is produced by intestinal microbiota and is usually enough to cover the daily requirements. It is fat soluble and stored in the liver. If your gut flora is disturbed by FUT2 genes, elevated glutamate, gluten sensitivity, and you have used the drug Warfarin or antibiotics, your K2 requirements may be higher.

Vitamin K2 deficiency is linked to arterial calcification, osteoporosis and poor dental health. This is why long-term use of anticoagulants like Warfarin are linked to accelerated bone loss and bone mass. Recent research has shown that vitamin K2 plays a role in having an inhibitory effect on breast cancer cells.

Polymorphisms in VOKRC1 have been linked to higher rates of arterial calcification and may increase the need for vitamin K2. To paraphrase one study, "A lifelong decreased activity of the VKORC1 enzyme may increase the risk of vascular calcification and could be further worsened by reduced intake of vitamin K2."

Polymorphisms in VOKRC1\*2 may increase the sensitivity to Warfarin dosing and vitamin K recycling. VKORC1\*2 appears to be the most important in relation to the variability in response to oral anticoagulants and the risk of excessive bleeding. Vitamin K2 has also been found in studies to be inhibited by statin drugs.

# CARDIOVASCULAR HEALTH AND ATHLETIC PERFORMANCE

## Power and Recovery-**ACTN3**

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ACTN3 rs1815739	Heterozygous TC

### Recap

 Improves ACTN3 Gene Function: Not applicable for ACTN3.

 Decreases ACTN3 Gene Function: Not applicable for ACTN3.

## POWER AND RECOVERY-**ACTN3**

The T (R) allele is associated with enhanced strength and training adaptation, improved protection from eccentric training-induced muscle damage, lower risk of sports injury, and reduced frailty in the elderly. Testosterone levels were also higher in male and female athletes with at least one R allele compared to the XX genotypes. When stratified by race and gender for power athletes in a 2019 meta-analysis, Asian and male athletes benefited the most from the RX (TC) genotype.

The ACTN3 RR and ACTN3 RX groups have not been significantly different, indicating that the presence of one or two R alleles does not have a dose-dependent effect on 200-meter sprint speed in elite athletes. However, there was some evidence for a dose-effect of the ACTN3 R allele and 200-meter sprint speed in elite male African athletes. The ACTN3 RR individuals had (on average) a faster best personal sprint time than ACTN3 RX individuals.

Having the RX genotype may represent the best of both worlds for cold adaptation, longevity, strength training, and exercise recovery.

## VO2 Max-**PPARGC1A**

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
PPARGC1A rs8192678	Homozygous TT

### Recap

 Improves PPARGC1A Gene Function: Aerobic exercise, cold water exposure, ashwagandha and eleuthero root.

 Decreases PPARGC1A Gene Function: Sedentary lifestyle.

## VO2 MAX-**PPARGC1A**

**Research:** Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PPARGC1A) is a master regulator of mitochondrial biogenesis, mitochondrial respiration, skeletal muscle fiber transformation (from fast to slow twitch), glucose and fatty acid metabolism, and the anti-oxidation machinery. PPARGC1A is expressed in cell types with high oxidative function (heart, skeletal muscle slow twitch fibers, liver, and pancreas) and in brown adipose tissue.

Several studies have shown that SNPs in PPARGC1A are associated with a significant lower level in aerobic power (i.e., VO2 max) in insulin resistant and untrained individuals as well as in athletes. Healthy untrained adults display a large individual variation in VO2 max that ranges from -20% to more than 50%.

Research indicates that the exercise-induced variation in VO2 max is 47% explained by genetics. If you have heterozygous or homozygous variants in PPARGC1A, you may have a naturally lower VO2 max for aerobic exercise and increased CRP (C-reactive protein) levels.

To increase VO2 max, consider cold exposure. Since mitochondria are what give us the ability to use oxygen in order to produce cellular energy, the more we have the more the aerobic potential.

Cold exposure activates the PPARGC1A gene and PGC1 $\alpha$  protein, which makes more mitochondria in the muscle. One study found that 15 minute exposure to cold water (50°F or 10°C) following high intensity running, increases PGC1 $\alpha$  in muscle tissue. Another study found that men that were immersed in cold water at 50°F (10°C) for 15 minutes, 3 times a week for four weeks after running were able to increase mitochondrial biogenesis occurring in their muscle tissue.

Adaptogens are another way to increase your VO2 max. One study found that ashwagandha increased velocity, power, VO2 max, lower limb muscular strength and neuromuscular coordination. A second study used elite Indian cyclists for 8 weeks. One group received 500mg of the root extract 2x a day, while the other group received a placebo. There was significant improvement in the experimental group in all parameters, namely, VO2 max and time for exhaustion on treadmill.

A study using eleuthero root found that using 800mg for 8 weeks increased VO2 max of by 12%, endurance time improved 23%, the highest heart rate increased 4%, and metabolism was altered which spared glycogen storage. The study concluded that "this was the first well-conducted study that shows that 8-week ES supplementation enhances endurance capacity, elevates cardiovascular functions and alters the metabolism for sparing glycogen in recreationally trained males."

## Muscle Injury-COL1A1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
COL1A1 rs1800012	Wild Type CC

## Recap



Improves COL1A1 Gene Function: Vitamin C, zinc, copper, glycine, proline, lysine and B6 (all precursors to collagen production) and cryotherapy.



Decreases COL1A1 Gene Function: Deficiencies in vitamin C, zinc, copper, glycine, proline, lysine, B6 and excessive NSAID use.

## MUSCLE INJURY-COL1A1

**Research:** According to one study, the gene encoding for the alpha1 chain of type I collagen (COL1A1) has been shown to be associated with cruciate ligament ruptures and shoulder dislocations.

You have the CC genotype for COL1A1, which lowers the production of Type 1 collagen. Approximately 90% of collagen in the body is Type I. Type I collagen is found in the skin, tendons, corneas, lungs and in 95% of bone.

ACL ruptures are considered the most severe injury sustained in sports. The A variant produces more COL1A1. Two AA's reduced risk of ACL rupture by ten times, while only 5% of the population have two AA's.

Cryotherapy has been shown to inhibit harmful collagenase (activity on collagen enzyme that breaks down collagen) and also decreased the production of inflammatory E2 series prostaglandins. For athletes, cryotherapy post-training could be a useful tool to help prevent injuries.

## Pesticides, HDL and LDL-PON1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
PON1 rs662	Heterozygous TC

## Recap



Improves PON1 Gene Function: Organic foods, calcium, magnesium, boron, lycopene, alpha-lipoic acid, gamma-linolenic acid (black cumin seed oil), broccoli sprouts, vitamins E, B1, B2, B5, B6, selenium, omega 3 fatty acids, high quality olive oil, polyphenols, naringenin, quercetin, pomegranates and alcohol in moderate amounts (1 drink for women and 1-2 drinks for men).



Decreases PON1 Gene Function: Pesticides, proton pump inhibitors, mercury, calcium deficiency and high homocysteine.

## PESTICIDES, HDL AND LDL-PON1

**Research:** Paraoxonases (PON1) are a family of enzymes involved in breaking down chemicals including several types of pesticides and pharmaceutical drugs. They are involved in protecting both high and low-density lipoproteins from oxidation, an important mechanism in atherosclerosis and heart disease. The rs662 SNP is the most clinically relevant for PON1. The C allele is also known as the "R" allele in research studies and is connected to atherosclerosis and heart disease.

A 2018 meta-analysis found that carriers of the variant R allele had higher levels of oxidized LDL, triglycerides, total cholesterol, and low-density lipoprotein cholesterol than the non-carriers. This was most pronounced in Asians and coronary heart disease patients. The hypothesis is that decreased levels of PON1 activity may lead to increased circulating levels of oxidized LDL and reduce the capacity of PON1-mediated inhibition of LDL-C oxidation.

Mercury appears to decrease PON1 function and liver expression of the PON1 gene is down-regulated in mice with high homocysteine. The proatherogenic effects of homocysteine may involve decreased serum PON1 activity, leading to impaired antioxidant function and decreased capacity to degrade homocysteine thiolactone.

The availability and catalytic activity of PON1 are impaired in many children with Autism Spectrum Disorders, making them more susceptible to the toxic effects of pesticide residues which are most frequently found on grain.

The rs662 SNP is the most clinically relevant for PON1. You need to make sure you are focusing on foods and drinks that improve gene function.

All of the vitamins, minerals, and compounds in the "Improves PON1 Gene Function" section have been verified in research to improve PON1 function. One way that pomegranates protect cardiovascular health is by augmenting nitric oxide. In one study, pomegranates protected against atherosclerosis by reducing LDL's basal oxidative status by 90%.

Moderate drinkers can also rejoice. Research has found that alcohol in small amounts (1 drink for women, 1-2 for men based on weight), improved PON1 activity by 395%. However, too much alcohol decreased PON1 by 45%.

A recent study found that red wine induced significant increases in plasma total antioxidant status and significant decreases in plasma MDA (inflammation biomarker). The results show that the consumption of 400 mL/day (14 ounces) of red wine for two weeks, significantly increases antioxidant status and decreases oxidative stress in the circulation.

Non-organic wine in particular may have concentrated amounts of additives, pesticides, insecticides and fungicides, while beer that uses GMO crops may be high in glyphosate (RoundUp). Residual concentrations of many different pesticides that have been detected in bottled wine were similar to initial concentrations on the grapes. The US and France are heavier users of pesticides. Italy and Argentina have been found to have wine most likely free from pesticides and heavy metals.

## Caffeine-CYP1A2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP1A2 C164A rs762551	Heterozygous AC

## Recap



Increases CYP1A2 Gene Function: A higher cruciferous vegetable intake may help increase caffeine metabolism for those with the CC slow metabolizer genotype, along with exercise.



Decreases CYP1A2 Gene Function: Oral contraceptives.

## CAFFEINE-CYP1A2

You have the heterozygous AC genotype and are considered an “intermediate metabolizer” of caffeine. This means that you do not metabolize caffeine slowly or quickly.

If you are female and taking oral contraceptives, this may reduce the clearance of caffeine. Research has shown that oral contraceptives significantly prolong the half-life of caffeine from 6.2 hours to 10.7 hours.

It is important to review your COMT gene function to better understand a sensitivity to coffee intake.

## Triglycerides-FADS1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
FADS1 rs174546	Homozygous TT

## Recap



Improves FADS1 Gene Function: Higher intake of the omega-3 fatty acids EPA and DHA.



Decreases FADS1 Gene Function: Low intake of EPA and DHA.

## TRIGLYCERIDES-FADS1

**Research:** Variants in the FADS1 SNP (rs174546) are associated with elevated triglyceride levels, which appears to be due to a higher need for EPA and DHA from animal foods. Studies have found that plasma triglyceride levels were lower in wild-type CC genotype when compared to carriers of the minor T allele.

Population average triglyceride levels have increased since 1976 in parallel with the constant growing epidemic of obesity, insulin resistance and Type-2 diabetes. A meta-analysis of 17 population-based prospective trials including 46,413 men and 10,864 women identified plasma triglycerides levels as an independent risk factor of cardiovascular disease.

Triglycerides are essentially fat in the blood that are driven by excess sugar and carbohydrate consumption. They are the driving force behind lipoprotein particles that are potent causes of heart disease, such as small LDL and very low-density lipoprotein (VLDL).

Numerous studies have found that omega-3 fatty acids administered as fish oil supplements lowers plasma triglyceride levels by 25% to 34%. While fish oil is known to lower triglycerides, there doesn't appear to be a difference in the FADS1 genotype response to supplementation. Looking at your NO3 gene function would be helpful in determining your fish oil response with elevated triglycerides.

A meta-analysis of 13 randomized controlled trials found that 500mg of vitamin C resulted in a significant decrease in serum LDL cholesterol and triglyceride concentrations.

## Potassium and Magnesium-ADD1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ADD1 rs4961	Heterozygous TG

### Recap



Improves ADD1 Gene Function: Lower sodium intake, magnesium, potassium, calcium, garlic, vitamin D and omega-3's.



Decreases Gene Function: High sodium intake, excess weight, high sugar intake, sedentary lifestyle, smoking and stress.

## POTASSIUM AND MAGNESIUM-ADD1

**Research:** A meta-analysis of 33 studies with 40,432 participants found that variants in rs4961 was significantly associated with hypertension in Asians. Other research found that carriers of the risk (T) allele responded better to diuretics and sodium-restricted diets, in that they tended to lower their blood pressure by ~ 10 mmHg points compared to rs4961(GG) homozygotes similarly treated.

Excess weight, high sugar intake, sedentary lifestyle, smoking, stress and high sodium intake all raise blood pressure. People living at higher latitudes throughout the world are at higher risk of hypertension, and patients with cardiovascular disease are often found to be deficient in vitamin D. Magnesium, potassium, calcium, vitamin D, garlic and omega-3's all lower blood pressure.

One study found that increasing potassium-rich foods to 4.7 grams was equivalent to cutting out 4 grams of sodium in terms of reducing blood pressure.

In another study, aged garlic extract given at a dose of 600-1500mg was just as effective as the drug atenolol in reducing blood pressure over a 24-week period.

## Blood Pressure-ACE2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ACE2 A8790G rs2106809	Homozygous GG

### Recap



Improves Gene Function: Vitamin D, potassium, curcumin, and resveratrol.



Decreases Gene Function: Smoking and a high saturated fat diet of over 50% of total calories.

## BLOOD PRESSURE-ACE2

Both angiotensin I converting enzyme 2 (ACE2) and the transmembrane protease, serine 2 (TMPRSS2), are crucial for SARS-CoV-2 entry into host cells. While ACE2 is the primary receptor for the spike protein (coronaviruses are known for their crown of spikes) of both SARS-CoV and SARS-CoV-2, mediating viral attachment to target cells, TMPRSS2 cleaves the spike protein. TMPRSS2 allows the fusion of viral and cellular membranes. This process is similar to viral activation and cell entry of other coronaviruses as well as influenza H1N1.

The expression of ACE2 has been detected in nasal epithelial cells, alveolar epithelial type II cells of lungs, and the luminal

surface of intestinal epithelial cells. The nose, lungs, and intestine facilitate viral entry and serve as a potential site of viral invasion. However, it appears the expression of TMPRSS2 determines the ability of the virus to enter the cells.

Research has suggested that age, sex, and genetic variants in the ACE2 gene can potentially affect ACE2 levels. Children generally have higher levels of ACE2 than adults. Women have been found to have higher ACE2 levels than men due to the upregulation of ACE2 by estrogen. Estrogen levels could be the foundational reason men and post-menopausal women are more susceptible to COVID-19.

One study of 534 subjects found that 67% of the variation in circulating ACE2 could be accounted for by genetic factors. Among different polymorphisms, it has been speculated that ACE2 rs2106809 might exhibit primary effects on the ACE2 levels. The circulating ACE2 levels tend to be greater in AA or AG genotype compared with the GG genotype.

A clinical study of 3408 patients found that ACE2 rs2106809 G allele conferred a 1.6-fold risk for hypertension in Chinese women. An Indian study confirmed this finding, and it found that ACE2 rs2106809 polymorphism was associated with hypertension in both females and males.

Potassium, vitamin D, and resveratrol all increase ACE2 expression. Betulinic acid (chaga mushroom) and oleanolic acid (olive oil) have also been studied as SARS-CoV-2 entry inhibitors. Research has also found that curcumin binds to receptor-binding domain site of viral S protein and also to the viral attachment sites of ACE2 receptor and downregulates TMPRSS2, demonstrating that curcumin can act as potential inhibitory agent antagonizing the entry of SARS-CoV2.

# DNA PROTECTION, DAMAGE & REPAIR

## Prostate-ESR2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ESR2 rs2987983	Heterozygous AG

## Recap



Improves ERS2 Gene Function: Phytoestrogen foods, milk thistle, apigenin, and iodine.



Decreases ERS2 Gene Function: Obesity, BPA plastic, unfiltered tap water, atrazine (sprayed on golf courses, lawns, non-organic corn and non-organic wheat), dioxins (bleached products, non-organic animal fats) and phthalates (many chemically-based personal care products).

## PROSTATE-ESR2

The ER-beta estrogen receptor has features of a tumor suppressor gene and is strongly expressed in the breast, bone, cardiovascular system, uterus, bladder, prostate, lung, ovarian cells, and testicular cells.

ERS2 is highly expressed in the prostate, and the expression declines when the prostate becomes enlarged and with cancerous prostate cells. Dietary phytoestrogens are a consistent source of debate for health benefits and concerns in the scientific community for men and women. Phytoestrogens can bind to estrogen receptors and exert both estrogenic and anti-estrogenic effects depending on the tissue, and the signaling pathways differ from estrogen.

In a case-control study in Sweden from 2006, the overall decreased risk of prostate cancer of carriers of the variant allele of ESR2 (rs2987983) was almost 60% with a high phytoestrogen dietary intake (but not lignans) compared to men with a low phytoestrogen intake, whereas no such association was found among men with the wild-type genotype.

Phytoestrogens can both bind to estrogen receptors and stimulate sex hormone-binding globulin (SHBG) production, changing the amount of 17 $\beta$ -estradiol or testosterone in circulation. Phytoestrogens are also able to inhibit proteasome, which appears essential for breast cancer cell survival. Apigenin - a flavonoid found in celery and parsley - has been found to be capable of inhibiting proteasomes, leading to the stabilization of ERS2 and apoptosis of prostate cancer cells.

The main sources of phytoestrogens in the study were flaxseed, rye bread, wheat bread, cereals, berries, soy, and other beans. Researchers concluded that phytoestrogens and the ERS2 gene interact synergistically in a fraction of the population with the heterozygous or homozygous genotype (rs2987983) by repressing androgen receptors, inhibiting androgen-driven proliferation.

Iodine modulates the estrogen pathway and research has shown that there is a low incidence of cancers of the prostate, endometrium, ovary, and breast in populations consuming diets with a high iodine content. Additionally, a German study performed on men with prostate cancer found a significant inverse relationship between vitamin K2 consumption and advanced prostate cancer.

A combined analysis of CYP1A1, CYP1A2, CYP3A4, CYP1B1, SHBG, and COMT could give more insight into individual estrogen metabolism.



# METHYLATION CYCLE

## Folate-MTHFR 1298

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
MTHFR 1298 rs1801131	Heterozygous TG

### Recap

 Improves MTHFR 1298 Gene Function: Vitamin C, L-arginine, folate, B6, magnesium, holy basil, selenium, royal jelly and deep breathing techniques.

 Decreases MTHFR 1298 Gene Function: Chronic stress, oral contraceptives, high levels of mercury, arsenic, lead and aluminum, synthetic folic acid, phenylalanine, aspartame, oxidative stress and high protein diets.

## FOLATE-MTHFR 1298

The heterozygous MTHFR 1298 has a reduced function of approximately 20%. If you have the heterozygous MTHFR 1298 and a heterozygous MTHFR 677, you may have elevated homocysteine levels and may require a higher folate intake (400-800 mcg).

One study in 259 post-menopausal women found that for those with variants in CYP1B1 (rs1056836), KRAS (rs61764370) and MTHFR (rs1801133 and rs1801131), oral contraceptives and hormone replacement therapy was associated with shorter leukocyte telomere length. Shorter leukocyte telomeres are connected to premature aging, and may increase the risk of cancer, cardiovascular disease, obesity, diabetes, chronic pain, and sensitivity to perceived psychological stress.

On its own, the heterozygous MTHFR 1298 genotype may not pose any issues with adequate folate intake, however vitamin C, L-arginine, folate, B6, magnesium, holy basil, selenium, royal jelly and deep breathing techniques will help healthy MTHFR 1298 gene function.

## Magnesium-MAT1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
MAT1 rs2993763	Heterozygous AG

### Recap

 Improves MAT1 Gene Function: Methionine, magnesium, boron, folate and betaine

 Decreases MAT1 Gene Function: Smoking, sugar, chronic stress, high alcohol intake, coffee, tea, fluoridated water, phosphoric acid, non-fermented grains, intense exercise, high protein diets, high calcium supplementation, high arsenic levels, antacids, proton pump inhibitors, ACE inhibitors, birth control, hormone replacement therapy, Estradiol, Premarin, antibiotics, antivirals, immunosuppressants, methylphenidate, Tamoxifen and corticosteroids.

## MAGNESIUM-MAT1

**Research:** Methionine adenosyltransferases (MATs) produces S-adenosylmethionine (SAME) via an ATP-driven process. SAME donates methyl groups to all the neurotransmitters and functions as an anti-depressant. Approximately 95% of SAME is used in methylation reactions that influence the activity of DNA, RNA, proteins, phospholipids, hormones, and neurotransmitters. High arsenic levels may deplete SAME.

Variants in the MAT1 genes may lead to lower SAmE levels. Plasma SAmE concentrations were lower in subjects carrying the variant allele of MAT1A rs2993763 only in men when methionine was low. Elevated COMT levels will draw heavily on MAT1A, also showing a magnesium connection.

ATP is highly dependent on magnesium, and therefore variants in MAT1A may increase the need for magnesium if deficiency is present to produce sufficient SAmE along with methionine. Plasma folate and betaine concentrations were positively associated with plasma SAmE concentrations only in men.

Depleted levels of SAmE have been implicated in many of the disorders that can be beneficially affected by intakes of boron of greater than or equal to 3 mg/d, including arthritis, osteoporosis, cancer, diabetes, and impaired brain function.