



# Welcome to the future of health and human potential

NAME: TEST ACCOUNT

DATE: SEP 26, 2022



myDNA is an accredited laboratory with NATA approved Lab services based in Melbourne Australia and a CLIA certified and CAP accredited Lab in Houston Texas.

Each sample is run on parallel arrays that have been analytically validated.

This analysis does not provide information on genetic carrier risk profiles and is not intended to diagnose a disease.

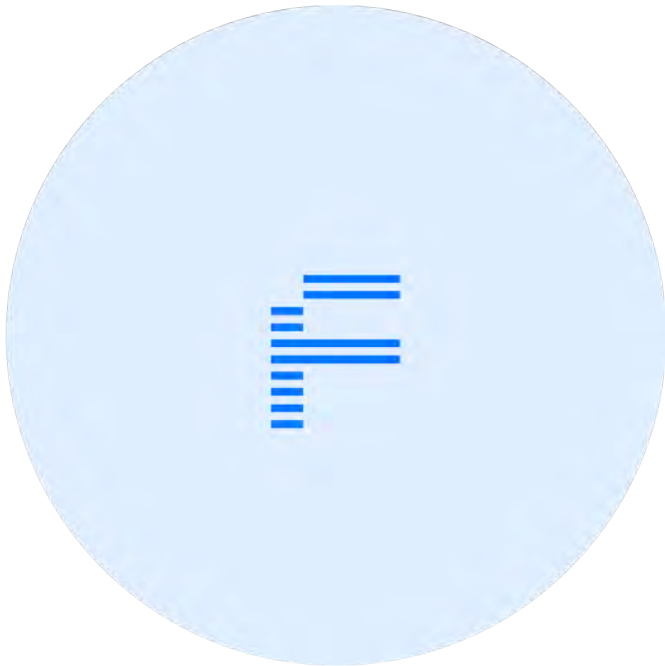
For further information please contact Lab Services partner NutriPATH on 1300 688 522

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# MACRONUTRIENT METABOLISM

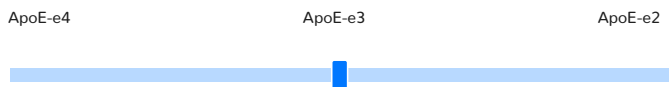
## APOE STATUS : 3/3



**You are a ApoE-e3**

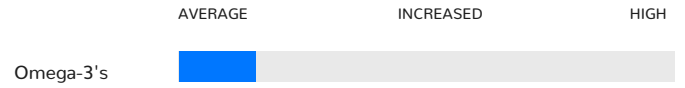
Apolipoprotein E (ApoE) is a lipid-binding protein that transports triglycerides and cholesterol in multiple tissues, including the brain. The e4 allele is common in hunter-gatherer communities, while the e3 and e2 alleles are most common in agricultural communities.

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## FAT REQUIREMENTS

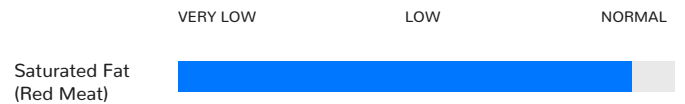
[Eat Less](#) [Eat More](#)



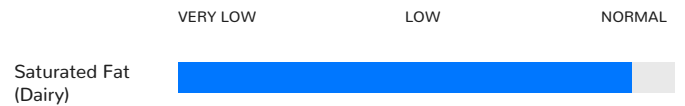
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## PROTEIN REQUIREMENTS

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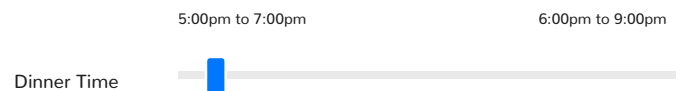


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## MEAL TIMING



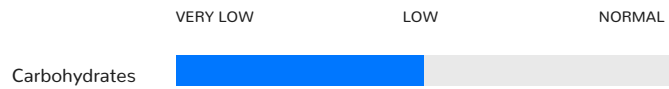
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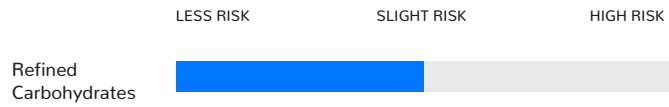
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# CARBOHYDRATE REQUIREMENTS

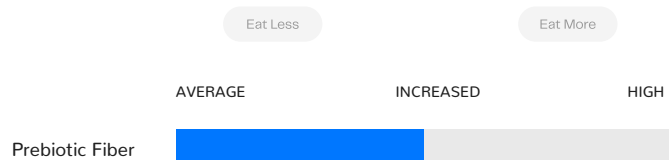


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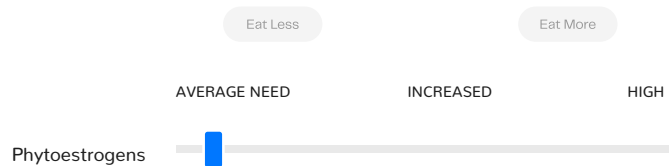
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# FIBER REQUIREMENTS

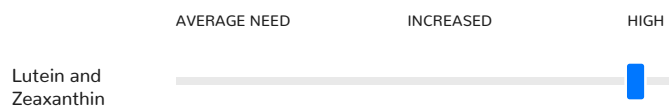


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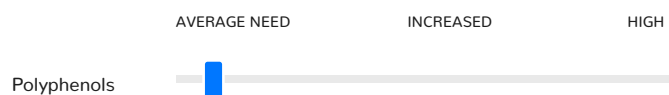
# PHYTONUTRIENT REQUIREMENTS



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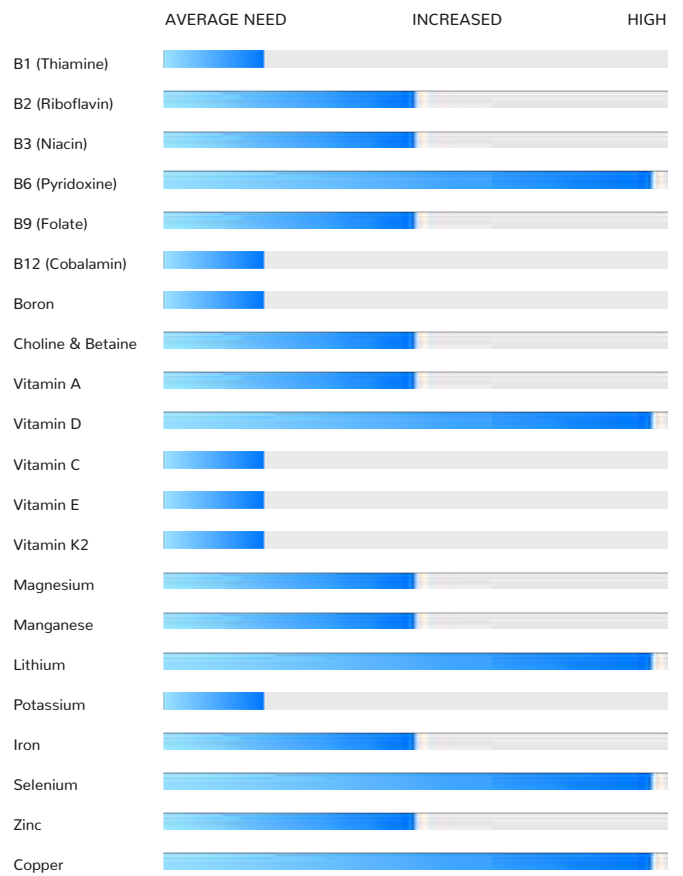


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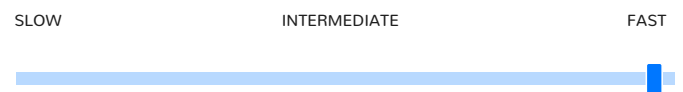


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# MICRONUTRIENT REQUIREMENTS



# CAFFEINE METABOLISM



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Cinnamon



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AVERAGE NEED      INCREASED      HIGH

Cruciferous  
Vegetables



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AVERAGE NEED      INCREASED      HIGH

Lycopene



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AVERAGE NEED      INCREASED      HIGH

Apigenin (Males)



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AVERAGE NEED      INCREASED      HIGH

Resveratrol

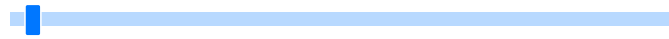


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## LACTOSE TOLERANCE

TOLERANT

INTOLERANT

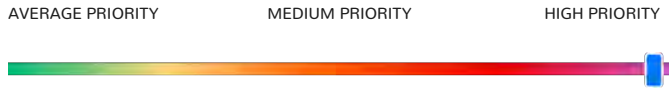


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## TOXIN SENSITIVITY

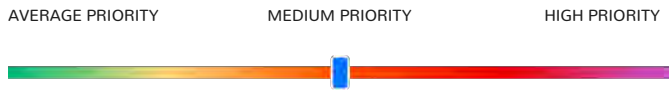
Mycotoxins

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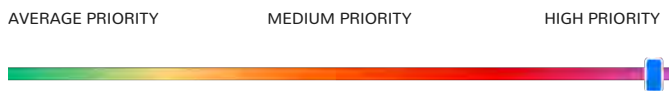
Xenoestrogens

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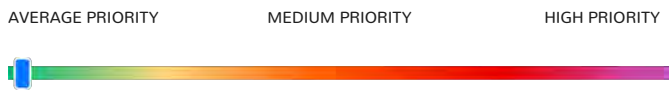
Occupational Toxins

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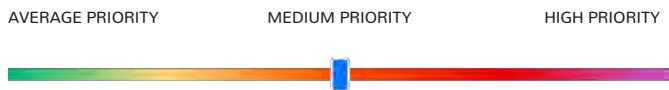
Ethanol

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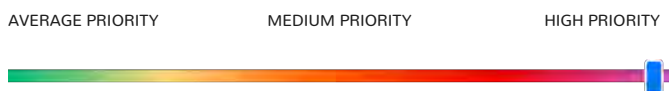
Formaldehyde

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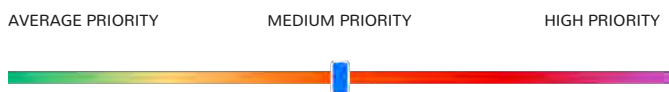
Benzo(a)pyrene

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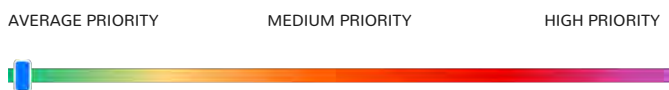
Aromatic Amines

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Benzene

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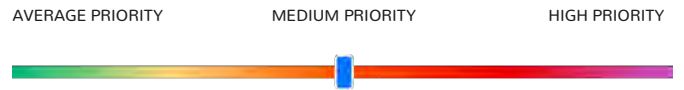
Aspartame

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## PESTICIDES, HERBICIDES AND HEAVY METAL SENSITIVITY

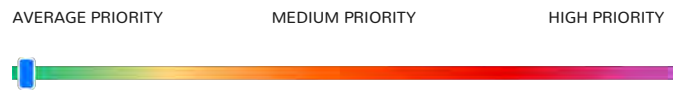
Glyphosate

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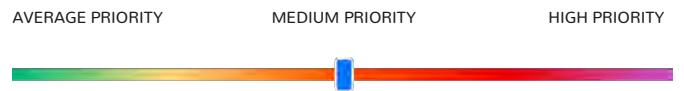
Organochlorines

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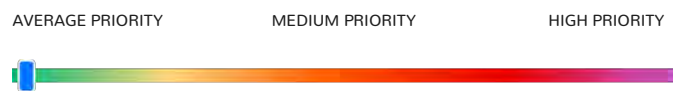
Organophosphate Insecticides

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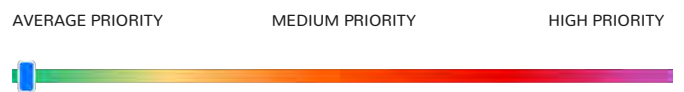
Arsenic

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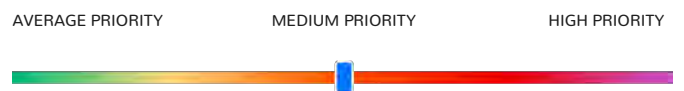
Cadmium

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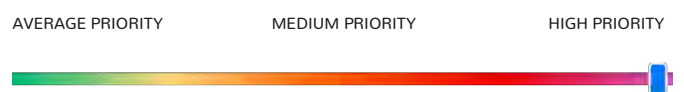
Mercury

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Lead

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AVERAGE PRIORITY

MEDIUM PRIORITY

HIGH PRIORITY



Food Dyes

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AVERAGE PRIORITY

MEDIUM PRIORITY

HIGH PRIORITY

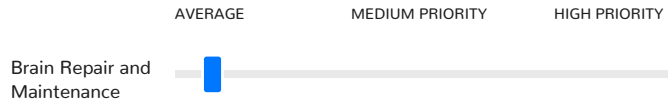




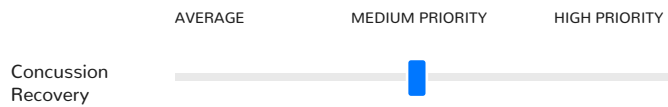


# MENTAL HEALTH & COGNITIVE PERFORMANCE

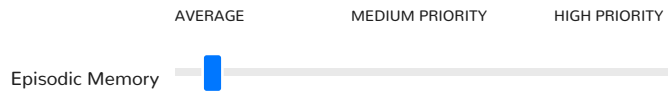
## MENTAL HEALTH AND COGNITIVE PERFORMANCE



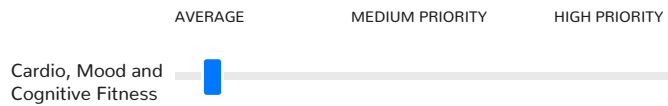
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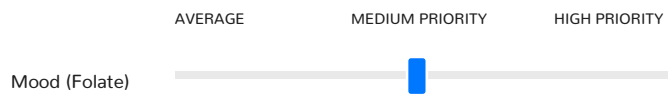
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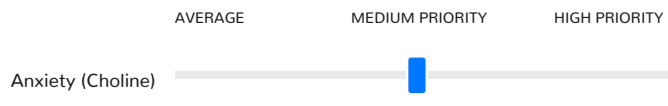
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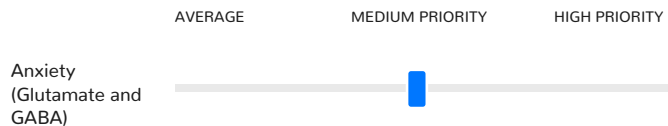
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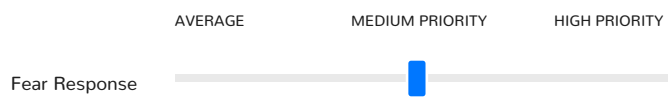
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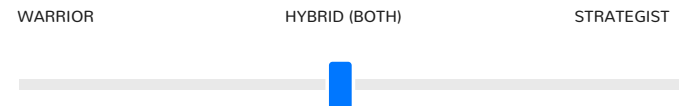
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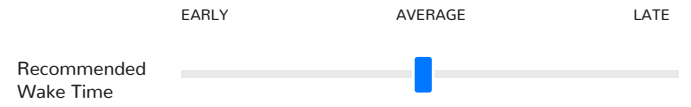


## WARRIOR OR STRATEGIST (COMT)

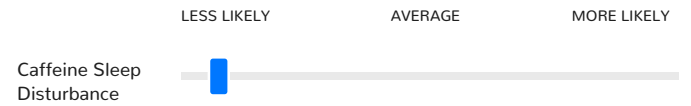


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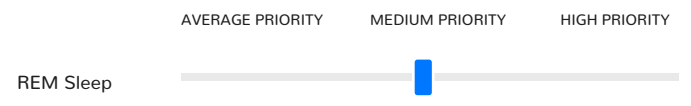
## SLEEP SUPPORT



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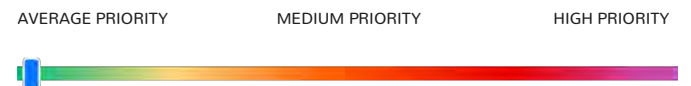


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## STRESS MANAGEMENT

Stress Perception

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Stress and Digestion

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AVERAGE      MEDIUM PRIORITY      HIGH PRIORITY

Addiction



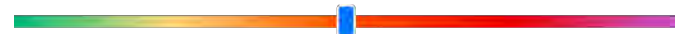
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LOW      MEDIUM      HIGH

Reward System



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Cardio and Stress Relief

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AVERAGE PRIORITY      MEDIUM PRIORITY      HIGH PRIORITY



Weight Training and Stress Relief

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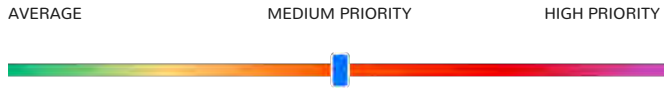
AVERAGE PRIORITY      MEDIUM PRIORITY      HIGH PRIORITY



## COVID-19

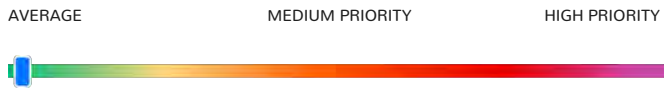
SARS-CoV-2 Susceptibility

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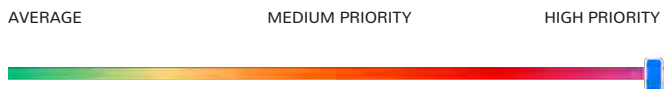
COVID-19 Viral Severity

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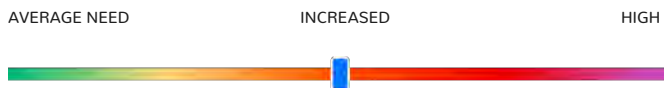
COVID-19 Lung Damage Severity

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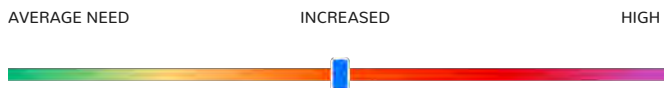
Glutathione

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Vitamin A

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Vitamin C

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Vitamin D

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Selenium

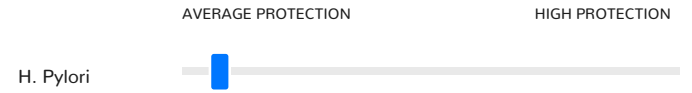
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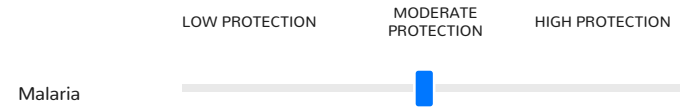
Zinc

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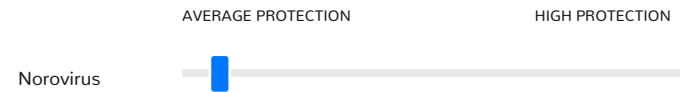
## BACTERIA, YEAST, PARASITES AND VIRUSES



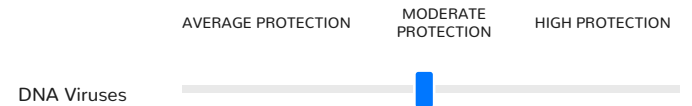
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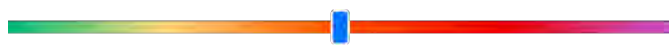


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AVERAGE NEED                      INCREASED                      HIGH



Copper

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LOW NEED                      AVERAGE NEED                      INCREASED



Iron

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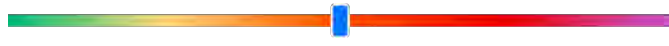
LOW NEED                      AVERAGE NEED                      INCREASED



B12

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AVERAGE NEED                      INCREASED                      HIGH



Folate

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AVERAGE NEED                      INCREASED                      HIGH



B6 (Pyridoxine)

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AVERAGE NEED                      INCREASED                      HIGH



Bifidobacteria

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AVERAGE NEED                      INCREASED                      HIGH



Glycine

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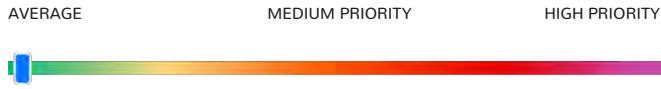
AVERAGE NEED                      INCREASED                      HIGH



## CARDIOVASCULAR HEALTH

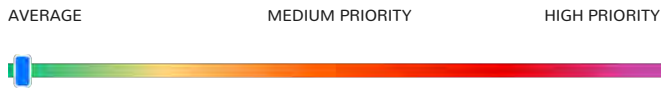
HDL and LDL

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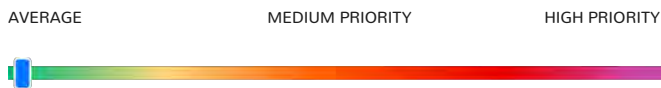
VLDL

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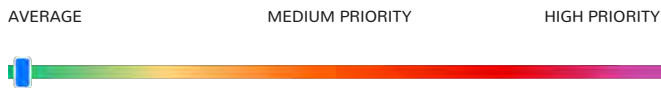
Triglycerides

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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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## EXERCISE



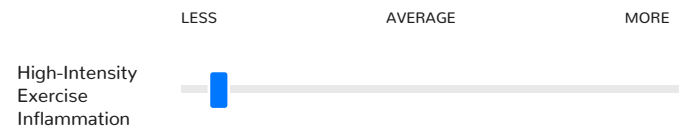
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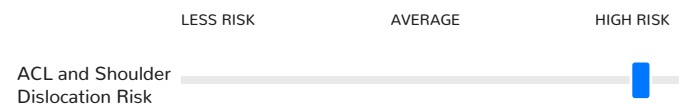
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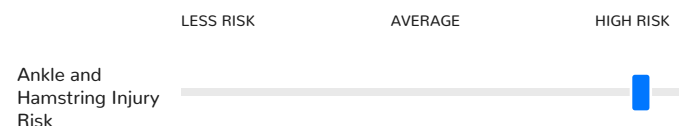
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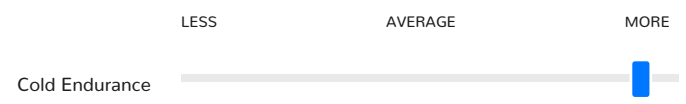
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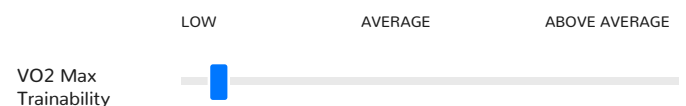
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AVERAGE                      MEDIUM PRIORITY                      HIGH PRIORITY



Blood Clots

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AVERAGE                      MEDIUM PRIORITY                      HIGH PRIORITY



Uric Acid

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AVERAGE                      MEDIUM PRIORITY                      HIGH PRIORITY



Hemochromatosis

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LESS LIKELY                      SLIGHT RISK                      MORE LIKELY



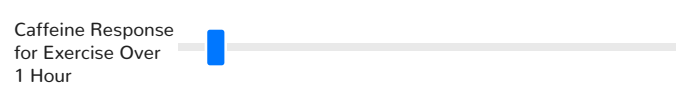
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LOW                      NO RESPONSE                      HIGH



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LOW                      NO RESPONSE                      HIGH

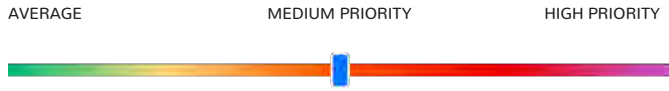


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## DNA PROTECTION & REPAIR

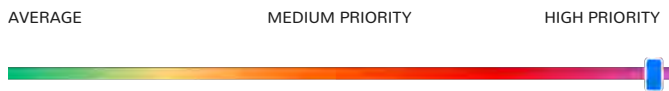
### Glutathione Protection

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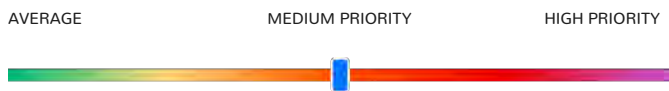
### Catalase Protection

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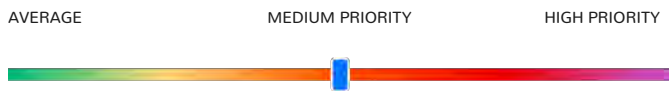
### Mitochondrial Protection

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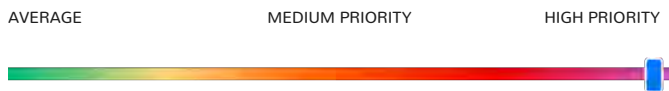
### UV Protection

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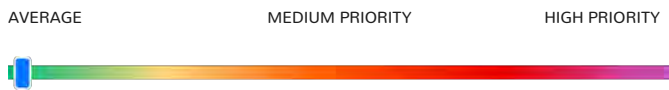
### Skin Protection

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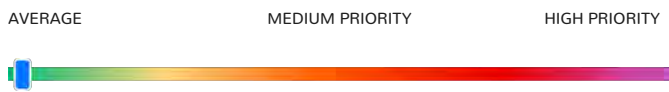
### Lung Protection

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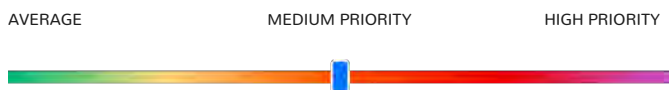
### Colon Protection

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### Cured Meat and Colon Health

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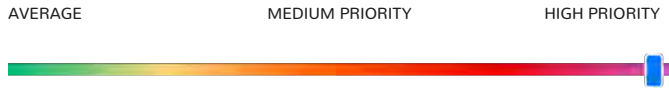
### Eye Protection

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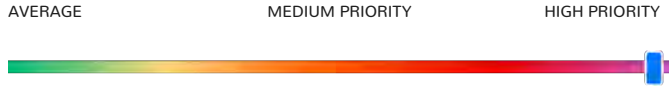
Thyroid Protection

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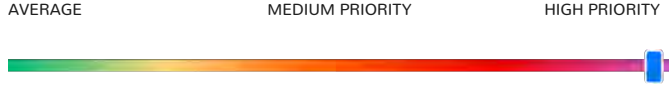
Pancreas Protection

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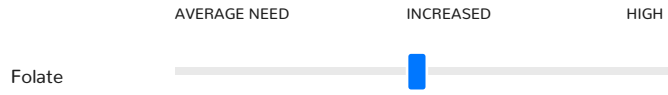
Bladder Protection

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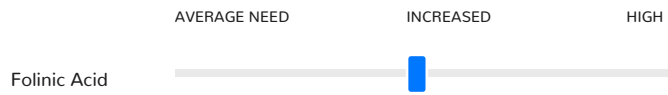




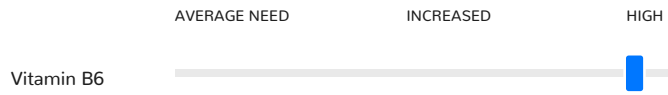
## METHYLATION



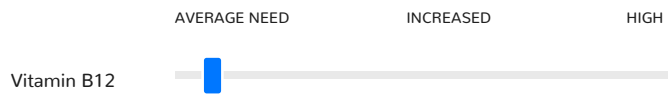
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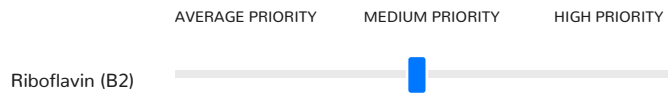
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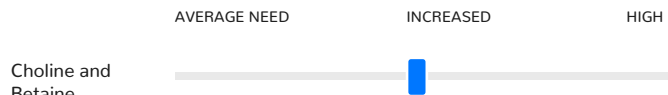
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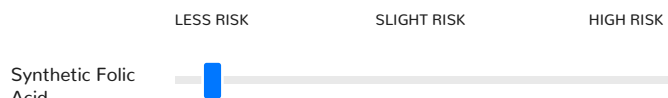
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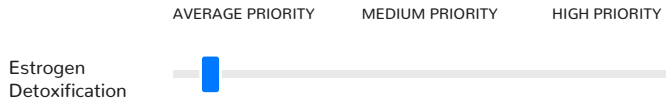


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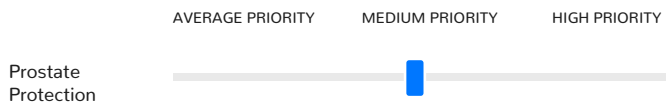


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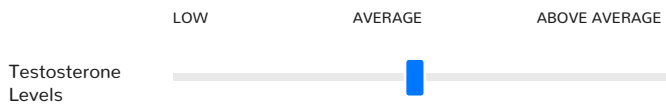
## HORMONE SUPPORT



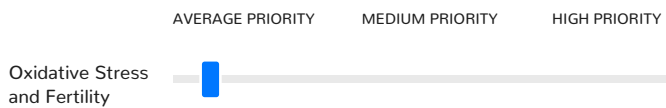
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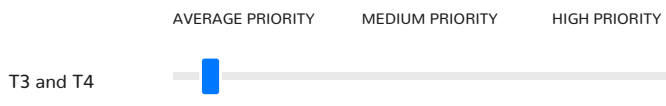
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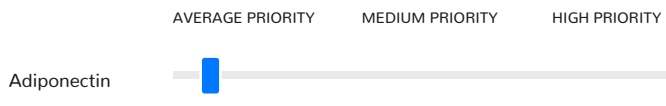
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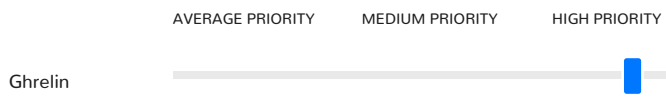
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This section is a thorough overview of your individual gene function across the entire analysis in just a few pages. If you are looking for a brief summary of the most important parts of your report without doing a deep dive into the genotype tables and clinical research sections, this is the place to start. Be proud of your inherent genetic strengths!

## DIGESTION

- = **ALA to EPA and DHA Conversion-FADS2** - Your genotype is associated with an improved conversion of plant-based omega-3 ALA (walnuts, flax seeds, pumpkin seeds) to EPA and DHA.
- = **Prebiotics, Probiotics and B12-FUT2** - The rs601338 FUT2 AG genotype in European, African, and Indian populations is associated with intermediate B12 levels and improved bifidobacteria populations in the gut compared to the AA genotype, increasing immune function against respiratory infections.
- = **Vitamin C-SLC23A1** - Your genotype is associated with improved whole-body vitamin C homeostasis through dietary absorption and renal reabsorption.
- = **Adiponectin-ADIPOQ** - Your genotype is associated with a higher probability of normal adiponectin levels, linked to improved bodyweight, insulin, and glucose levels.
- = **Iron** - Your genotype is associated with a lower risk of iron overload for the HFE C282Y gene. However, a heterozygous HFE C282Y and HFE H63D gene could change this result.
- = **Saturated Fat-PPAR-alpha** - You have the wild-type genotype that is associated with improved saturated fat metabolism and ketone body production during fasting. Assess your other fat metabolism genes for a more complete assessment.
- = **Fat Metabolism-ACSL1** - Your genotype is associated with improved glucose metabolism from saturated fat intake.
- = **Saturated Fat-APOA2** - Your genotype is associated with a reduced likelihood of saturated fats causing weight gain.
- = **Lactose** - You have the heterozygous AG genotype that is associated with a lower probability of lactose intolerance.
- = **Histamines-APB1** - You have the wild-type genotype that is associated with improved histamine breakdown in the digestive tract.
- = **Uric Acid-ABCG2** - Your genotype is associated with a lower probability of chronically elevated uric acid levels.
- = **Ethanol Metabolism-ALDH2** - Your genotype is less likely to experience facial flushing from alcohol due to improved acetaldehyde metabolism.

## DNA DAMAGE, PROTECTION AND REPAIR

- = **Prostate-ESR2** - For men with the ESR2 rs2987983 wild-type AA genotype, your genotype is associated with an improvement in tumor suppressor gene function for prostate health and lowering phytoestrogen requirements. All genes related to prostate health should be analyzed to better determine the cumulative value for prostate protection.
- = **DNA Repair-MDM2** - Your MDM2 genotype is associated with improved DNA repair for sun damage if you are female.
- = **DNA Repair-MLH1** - Your genotype is associated with improved DNA repair for colon, endometrium, lung, and brain protection.
- = **Longevity-SIRT1** - Your SIRT1 genotype is associated with normal SIRT1 activity for longevity. While not a weakness, you may want to increase SIRT1 activity epigenetically to increase the probability of longevity, especially if you have the APOE-e4 allele. A sedentary lifestyle, aging, poor diet, and obesity lowers SIRT1 activity. Exercise, fasting, 7-8 hours of sleep per night, saunas, polyphenols, vitamin D, omega-3 fatty acids, resveratrol, magnesium, and melatonin have all been found to increase SIRT1 activity.

## METHYLATION

- = **Folate-MTHFR 1298** - Your genotype is associated with improved BH4 levels and neurotransmitter function. Healthy BH4 levels assist in the management of cardiovascular health, mental health, and digestive health.
- = **Folate-DHFR** - Your genotype is associated with an improved breakdown of synthetic folic acid at the beginning of the folate cycle. However, variants in MTHFR 677 can also affect folic acid metabolism.
- = **B12, B2 and Zinc-MTR** - You may have improved MTR function, assisting homocysteine metabolism.
- = **B6-CBS** - Your genotype is associated with improved homocysteine and hydrogen sulfide levels, assisting gut repair and brain health.
- = **Arsenic-CBS** - Your genotypes are associated with improved arsenic metabolism and detoxification for the CBS genes.

## HORMONES

- = **Sex Hormone Binding Globulin** - If you are female, your genotype is associated with helping maintain normal estrogen and testosterone levels. Other epigenetic factors like obesity, fatty liver, and Type 2 diabetes should be considered when assessing SHBG levels.
- = **Testosterone-Men** - If you are male, your genotype is associated with improved total and free testosterone levels for the SHBG rs6258 gene.
- = **Thyroid-DI01** - Your genotype is associated with improved DI01 gene function for T3 and T4 thyroid function, however other epigenetic factors should be assessed.
- = **Thyroid-DI02** - Your genotype is associated with improved T3 and T4 thyroid function in the brain for the DI02 gene.
- = **Estrogen Metabolism-CYP1A1** - Your CYP1A1 wild-type genotype is improved for the beginning phase of estrogen metabolism. Please review all genes involved in estrogen metabolism for a complete picture of the process.
- = **Estrogen Metabolism-CYP2C19** - Individuals with the TT genotype for CYP2C19\*17 are considered the ultra-rapid metabolizer phenotype. This may positively add to the cumulative value for improving estrogen metabolism. Please review all genes involved in estrogen metabolism for a complete picture of the process.
- = **Estrogen Metabolism-CYP1A2** - For men and women with the CYP1A2 AA genotype, coffee intake was found to be more protective against estrogen receptor-positive breast cancer and prostate cancer.
- = **Estrobolome-FUT2** - Your heterozygous genotype is associated with improved bifidobacteria gut bacteria, assisting the gut phase of estrogen detoxification.

## NEUROTRANSMITTERS

- = **Serotonin Receptor-Memory** - You have the wild-type genotype that is associated with an improved episodic memory, which is the ability to recall details regarding personal experiences, names of people, specific events, and what exactly occurred.
- = **Serotonin Receptor-Stress** - You may have improved function for the serotonin receptor gene connected to perceived stress and the ability to regulate chronic stress. This may reduce the probability of low vagal tone, anxiety, depression, and obsessive and compulsive thoughts related to dysregulated serotonin levels.
- = **Dopamine, Adrenaline and Estrogen-COMT** - The heterozygous genotype for COMT V158M and H62H scored significantly higher on insight problem-solving tasks and had a greater ability for social facilitation and cooperativeness.
- = **Glutamate-BDNF** - Your genotype is associated with improved glutamate modulation, brain repair, spatial learning, memory, and adaptability.
- = **Cholesterol-APOE** - You have the ApoE e3/e3 genotype, improving cholesterol transport and the maintenance of brain neurons. The ApoE e3 allele improves cognitive fitness, HDL and LDL profiles, viral protection, and the response to plant bioactive compounds.

## ANTIOXIDANTS AND INFLAMMATION

- = **Glutathione-GSTM1** - While the GSTM1 null genotype has been associated with a greater sensitivity to benzo(a)pyrene, there is also a benefit to this genotype. The benefit is that the null genotype may retain a higher level of isothiocyanates, the anti-cancer compounds found in cruciferous vegetables that may also be required in higher amounts for this genotype.
- = **Glutathione-GSTP1** - You have the wild-type AA genotype for GSTP1 rs1695 that is associated with improved glutathione antioxidant protection for breast, lung, or prostate health; however, supplemental vitamin E as alpha-tocopherol may be inflammatory. Your GSTP1 rs1138272 genotype may increase or decrease this effect.
- = **Heavy Metals-GSTP1** - You have the wild-type CC genotype for GSTP1 rs1138272 that is associated with improved glutathione antioxidant protection against heavy metals, pesticides, and air pollution for colon, prostate, lung, throat, and fertility health. Your GSTP1 rs1695 genotype may increase or decrease this effect.
- = **Glutathione-CTH** - Your genotype is associated with improved gene function, leading to adequate cysteine for glutathione production.
- = **Nitric Oxide-NOS1** - Your genotype is associated with an average required intake of red, yellow, and orange vegetables to modulate the inflammatory process for NOS1.
- = **Nitric Oxide-NOS2** - Your NOS2A gene is functioning optimally for reducing the probability of age-related macular degeneration from cigarette smoke.
- = **Eye Health-ARMS2** - Your genotype is associated with a lower sensitivity to the negative effects of smoking on eye health.

## DETOXIFICATION

- = **Liver Enzyme-CYP1A1** - Your genotype is associated with improved detoxification of benzopyrene from cigarette smoke and will assist the function of your GSTM1 gene.
- = **Liver Enzyme-THC and CYP2C9** - You have the wild-type genotype that is associated with improved metabolism of THC, the active psychoactive compound in cannabis.
- = **Liver Enzyme-CYP2D6** - Your genotype is associated with improved metabolism of certain drugs associated with CYP2D6 rs1065852. However, more CYP2D6 SNPs are needed for a complete panel. Please talk to your doctor about further testing for CYP2D6 and drug metabolism.
- = **Liver Enzyme-CYP2E1** - Your genotype is associated with improved metabolism of benzene and acrylamide for colon health.
- = **Liver Enzyme-CYP3A4** - Your genotype is associated with normal metabolism of certain drugs that use this enzyme. We recommend further pharmacogenomic testing with your doctor for more information regarding CYP3A4.
- = **Aromatic Amines-NAT2** - You have the intermediate acetylator genotype for NAT2, which is associated with a reduced risk of bladder cancer in smokers and may improve the detoxification of aromatic amines found in commercial hair dyes, industrial and manufacturing plants, meat cooked at high temperatures, and diesel exhaust.
- = **Vitamin K2-VOKRC1\*2** - Your genotype is associated with normal vitamin K2 levels unless gut function is compromised from antibiotics, SIBO, leaky gut syndrome, IBS, IBD, Crohn's disease or parasites.
- = **Statins-COQ2** - Your genotype is associated with a lower likelihood of statin drug-induced muscle pain.

## CARDIOVASCULAR HEALTH AND ATHLETIC PERFORMANCE

- = **Power and Recovery-ACTN3** - You have the XX genotype found at higher latitudes and lower temperatures that appears to be selected for cold climate adaptation and endurance. The XX genotype also results in a deficiency of the ACTN3 protein that decreases elite sprint and power performance. However, this deficiency may represent a survival phenotype adapted to thrive in the cold.
- = **Muscle Recovery-IL6** - You have the GG genotype that is associated with lower levels of muscle inflammation post-exercise and improved recovery, faster sprint times, and is more common in sprint and power athletes compared to endurance athletes.
- = **LDL-LPA** - Your genotype is associated with healthy Lp(a) levels, a sticky form of LDL that affects plaque levels.
- = **Caffeine-CYP1A2** - You have the homozygous AA genotype and are a “rapid metabolizer” of caffeine. This means that caffeine will quickly be metabolized from your body and the effects lasting a shorter period of time. Variants in COMT can increase the sensitivity to catecholamines in coffee, and oral contraceptives can slow down caffeine metabolism.
- = **Triglycerides-FADS1** - You have the wild-type CC genotype that is associated with lower triglycerides.
- = **Blood Clots-F5** - Your genotype is associated with improved gene function for a lower probability of deep vein thrombosis.
- = **Stress-ADRB2** - You have the wild-type GG genotype for ADRB2 rs1042713 that is associated with a lower inflammatory response on the heart from chronic stress.
- = **Blood Pressure-ACE1** - Your genotype is associated with intermediate baseline ACE levels. If you are female, ACE levels may be lower. Depending on ACE2 levels, you may have a more balanced renin-angiotensin system for blood pressure.
- = **Blood Pressure-AGTR1** - You have the wild-type genotype, associated with a lower probability for high blood pressure, elevated triglycerides, elevated ApoB, and NAFLD from excess dietary fat and carbohydrate intake.
- = **Blood Pressure-ACE2** - Your genotype is associated with higher baseline ACE2, improving the balance between ACE1 and ACE2 for blood pressure, and potentially lowering the risk of COVID-19 severity. Other dietary habits and health issues could affect this result.
- = **Phytoestrogens-TMPRSS2** - You have the AA genotype that is associated with a lower expression of TMPRSS2 and may decrease the susceptibility to viral infections and prostate cancer (men).

Genes are not your destiny - they are your blueprint. Please understand that these weaknesses can be turned into strengths based on the personalized recommendations given below. Making strategic changes to diet, environment, stressors, and even relationships can have a profound effect on optimizing gene function. Aim to turn every weakness into a strength by giving attention to the proactive, customized dietary and lifestyle modification recommendations in this section!

## DIGESTION

- = **Beta Carotene to Vitamin A Conversion Rate-BCMO1** - Your BCMO1 genotype combination is associated with a reduced conversion rate of plant-based beta carotene (squash, sweet potatoes, carrots) to vitamin A. This increases your need for foods higher in vitamin A like eggs, cod liver oil, wild salmon oil and organ meats for skin, digestion, healthy eyes, lungs, and immunity.
- = **B6-NBPF3** - You are more likely to have low B6 levels due to variants in the NBPF3 gene, increasing the sensitivity to medications that deplete B6 (oral contraceptives, antibiotics, ACE inhibitors, antacids, proton pump inhibitors and more). You need to focus on increasing foods high in B6 like wild salmon, pistachios, avocados and potatoes.
- = **Ghrelin and Appetite-FTO** - Your genotype is associated with higher ghrelin levels (hunger hormone) that could lead to overeating and abdominal weight gain, especially when combined with variants in the ANKK1 gene. A focus should be on a protein and fiber-rich breakfast, monounsaturated and polyunsaturated fats, 7-8 hours of sleep per night, healthy vitamin D levels and aerobic exercise over 1 hour or high intensity exercise to stabilize ghrelin levels.
- = **Carbohydrates-TCF7L2** - Your genotype is associated with an increased probability of elevated blood sugar from refined sugar and grains. A diet low in refined sugar and flour, higher in protein and omega-3 fatty acids, glycine, diversified prebiotic foods, olive oil, cinnamon, turmeric, dark roast coffee and cordyceps mushrooms may be more beneficial.
- = **Stress and IBS-ADRB2** - You have the ADRB2 heterozygous CG genotype that is associated with a higher percentage of digestive disorders, IBS, and anxiety from elevated adrenaline levels. If you experience any of these, you may benefit from a deep breathing practice, meditation, yoga, vitamin C, and magnesium to modulate adrenaline levels.

## DNA DAMAGE, PROTECTION AND REPAIR

- = **DNA Repair-ATM** - Your genotype is associated with a higher need for folate to improve DNA repair in relation to pancreatic and breast (females) health.
- = **DNA Repair-TP53** - You have the heterozygous CG genotype that may be advantageous for fertility in cold climates, but also increases the need for selenium, zinc, vitamin C, reishi, and niacin for DNA repair against chemical toxicity to the thyroid gland and skin.
- = **Processed Meat and Colon Cancer-GATA3** - Your genotype is associated with a sensitivity to processed meats (hot dogs, salami, pepperoni) and colon cancer risk due to variants in GATA3. Reduce processed meat intake, optimize vitamin D levels and increase berries, apples, sauerkraut, broccoli, tomatoes, basil, rosemary, garlic, onions and leeks.



## METHYLATION

- = **Folate-MTHFR 677** - You have the heterozygous genotype that is associated with a reduced function of approximately 30%. This increases the need for riboflavin and methylfolate for normal homocysteine levels.
- = **Folate-MTHFD1 G1958A** - Your genotype is associated with an increased need for folinic acid, the second most common type of folate after methylfolate.
- = **B12-MTRR** - Your genotype is associated with a potentially higher sensitivity to B12 deficiency if there are variants in MTR as well.
- = **B12-TCN2** - Your B12 transportation may be affected if lithium levels are low due to your genotype in the TCN2 gene.
- = **Choline-PEMT** - Your genotype is associated with an increased need for dietary choline for liver health, normal homocysteine levels, breast health for women, and a healthy pregnancy for women.

## HORMONES

- = **Vitamin D-CYP2R1** - Your genotype is associated with low circulating vitamin D levels that can affect immunity, breast health in women, and testosterone levels in men. Check your vitamin D levels and make sure you are in range.
- = **Estrogen Metabolism-COMT** - For estrogen metabolism and detoxification, those with the intermediate AG COMT V158M genotype may have an increase in harmful estrogen metabolites that can cause DNA damage. To reduce the risk of these metabolites, you should avoid xenoestrogens, manage stress levels, maintain gut health, increase magnesium intake, and consume green tea polyphenols.
- = **MTNR1B-Melatonin** - You have the CG MTNR1B genotype, which is associated with delayed melatonin release, a longer duration of morning melatonin levels, and less insulin release during late night and early morning feeding. It is recommended to eat dinner early, avoid late night snacking and consume breakfast later in the morning for better glycemic control.

## NEUROTRANSMITTERS

- = **Dopamine, Adrenaline and Estrogen-COMT** - The heterozygous AG COMT V158M genotype is associated with a slower breakdown of dopamine, adrenaline, and estrogen, creating higher circulating levels in response to stress due to variants in the COMT genes. This may increase your need for magnesium, vitamin C, strength training, and sprints to reduce stress levels.
- = **Dopamine Receptors-ANKK1** - Your genotype is associated with a lower density of dopamine receptors, reducing dopamine targets within the striatum of the brain known for rewarding feedback. Lower dopamine targets could lead to a higher likelihood of addictive behaviors, compulsive eating, and ADHD. Getting 8 hours of sleep per night, keeping your blood sugar balanced with adequate protein and fiber, high-intensity exercise, lower media exposure, vitamin D, omega-3's, and meditation all increase dopamine receptor density.
- = **Histamines and Migraines-DAO** - The heterozygous CG genotype for DAO rs1049793 is associated with a slightly increased sensitivity to histamine-induced migraine headaches, especially in women. While not as impactful as the homozygous genotype, a histamine sensitivity could still occur.
- = **Anandamide-FAAH** - You have the common CC genotype that encodes for the fast activity of FAAH. This is associated with naturally lower anandamide levels that could increase anxiety, pain, pesticide sensitivity and a heightened stress response to threatening situations. You may benefit from aerobic exercise over 30 minutes (especially in altitude), CBD oil, red clover tea (women), kaempferol (raspberries, capers, cumin, cloves, almonds, cherry tomatoes, red wine), cacao, echinacea, rosemary, and hops to increase anandamide levels.
- = **Brain Health-PEMT** - Your genotype is associated with an increased need for dietary choline and daily walks for memory, anxiety, and REM sleep.
- = **Glutamate Transport-SLC17A7** - Your genotype is associated with delayed recovery from head injuries. We recommend also reviewing your APOE and BDNF genotype to determine cumulative impact. It is advised to be proactive with zinc, omega-3 fatty acids, Lion's Mane mushroom, magnesium and consistent exercise in case a head injury occurs.

## ANTIOXIDANTS AND INFLAMMATION

- = **Cell Protection-SOD2** - You have the heterozygous AG genotype for SOD2. Your mitochondria (powerhouse of the cell) may have a higher sensitivity to glyphosate, fluoridated water, chronic stress, poor sleep, and shallow breathing. Increase foods that contain manganese, lycopene, and vitamin C, milk thistle, mushrooms like reishi and cordyceps, and exercise that encourages deep breathing.
- = **Cell Protection-CAT** - Your genotype is associated with lower catalase levels and a sensitivity to BPA plastic and cell damage. This increases the need for foods high in flavonoids, the mushroom Lion's Mane, holy basil, cumin, anise, fennel, caraway, cardamom, and deep breathing practices to improve catalase levels.
- = **Glutathione-GSTM1** - You have the null genotype that is associated with a higher sensitivity to benzo(a)pyrene from the burning of wood or trash, tobacco smoke, asphalt, coal, diesel exhaust, charred meat, and gas cooking. If you have the GSTM1 null and NAT2 slow acetylator combination, that may affect lung, breast, bladder, skin, colon, and kidney health. It is recommended to increase your intake of cruciferous vegetables, vitamin C, vitamin E, vitamin A, milk thistle, resveratrol, curcumin, green tea, and white tea.
- = **Glutathione-GPX1** - Your genotype is associated with a higher need for selenium to combat oxidative stress and less tolerance to heat stress. Lower glutathione peroxidase increases the sensitivity to oxidative stress from low or high iron levels, statin drugs, thyroid damage, sun damage, and dietary or environmental lead exposure. Selenium, cold exposure, optimizing testosterone levels in men and estrogen in women, and adequate vitamin C, vitamin E, milk thistle, ginger, cumin, anise, fennel, caraway, and cardamom intake are all ways to assist GPX1.
- = **Eye Health-CFH** - Your genotype is associated with an increased need for lutein, zeaxanthin, bilberry, lingonberry, vitamin C, and vitamin E for healthy eyes.

## DETOXIFICATION

- = **Liver Enzyme-CYP1A2** - You have the AA genotype for CYP1A2 that is associated with a higher sensitivity to heterocyclic amines (fried meat) depending on if you have the homozygous null GSTM1 genotype or the NAT2 slow acetylator genotype. Marinades, unfiltered fermented drinks (Kombucha, beer, wine), cruciferous vegetables, parsley, and spinach have all been found to reduce the carcinogenic effect of heterocyclic amines.
- = **Liver Enzyme-CYP1B1** - You have the GG genotype that is associated with reduced detoxification of polycyclic aromatic hydrocarbons (highest in vegetable oils), oral contraceptives, cigarette smoke, an increased sensitivity to excessive sun exposure, and high-dose biotin supplementation. You can assist CYP1B1 with seaweed, celery, berries, rooibos tea, red wine, and dark roast coffee.

## CARDIOVASCULAR HEALTH AND ATHLETIC PERFORMANCE

- = **Power and Recovery-ACTN3** - You have the XX genotype that is associated with a reduced hypertrophy response to resistance training, increased post-exercise damage from eccentric training (lowering phase of a rep), and an increased risk of ankle and hamstring injuries. More attention may be needed for ankle and hamstring exercises to prevent injury, rest days in-between eccentric training, post-workout recovery strategies like cold-water immersion, and maintaining muscle mass later in life.
- = **VO2 Max-PPARGC1A** - Your genotype is associated with a higher need for more strategies to increase oxygen capacity for aerobic exercise, including a structured endurance program, cold exposure, and adaptogens. Your genotype in the GSTP1 rs1695 gene can also influence this result.
- = **Muscle Injury-COL1A1** - You have the wild-type CC genotype that is associated with an increased need for dietary collagen for healthy skin, tendons, corneas, lungs, and bones. Vitamin C, zinc, copper, glycine, proline, lysine, and B6 are all precursors to collagen production.
- = **Pesticides, HDL and LDL-PON1** - Your genotype is associated with decreased PON1 gene activity and reduced pesticide detoxification that could affect LDL oxidation. Elevated mercury levels and high homocysteine can further negatively affect PON1. There are numerous strategies to improve PON1 including choosing organic foods, adequate calcium and magnesium, pomegranates, broccoli sprouts, high-quality olive oil, and a glass of red wine.
- = **Raw Fruit and Vegetable Intake-9p21** - You have the heterozygous genotype that is associated with an increased need for phytonutrients from a higher raw fruit and vegetable intake for a healthy heart.
- = **Potassium and Magnesium-ADD1** - If you have Asian ancestry, your genotype is associated with an increased risk of a higher sodium intake causing elevated blood pressure. Increasing potassium, vitamin D, magnesium, calcium, garlic, and omega-3's all lower blood pressure.



# YOUR PERSONALIZED DNA-BASED GROCERY LIST

This section of the report represents the most expansive, actionable summary of what you can do, right now, to dramatically up-regulate gene function, building a happier, healthier you! No technical expertise is required - just make these recommendations non-negotiable when you visit the grocery store.

Your grocery list is generated based on a combination of unique gene variants that require an increased intake of the following vitamins, minerals, phytonutrients, amino acids, fiber and more. This list generates the foods and drinks based on the highest levels for each section and does not take into account any food allergies or sensitivities.



**B2**

Lamb, salmon, yogurt, liver and oyster mushrooms



**B6**

Wild salmon, yellowfin tuna, liver, chicken breast, unfiltered fermented drinks, pistachios, avocado, sweet potatoes, and spinach



**Beta-Carotene**

Sweet potatoes, carrots, spinach, squash, cantaloupe, and broccoli



**Betaine**

Spinach, shrimp, beets, and whole grain sourdough bread



**Copper**

Potatoes, shiitake mushrooms, cashews, sunflower seeds, dark chocolate, and shellfish



**Folate**

Collard greens, beets, black-eyed peas, raw spinach, asparagus, hummus, broccoli, romaine lettuce, parsley, liver, strawberries, oranges, and sprouted lentils



**Glucosinolates**

Brussels sprouts, mustard greens, turnips, savoy cabbage, kale, watercress, red cabbage, broccoli cauliflower, and Bok Choy



**Glycine**

Broth, collagen powder, meat with the skin, ribs, shanks, drumsticks, and baobab



**Lithium**

Mineral water, shellfish, tomatoes, spinach, unpeeled potatoes, eggplant, cabbage, rooibos tea, rosehips, pastured eggs and *Saccharomyces cerevisiae* (yeast)



**Lutein and Zeaxanthin**

Cooked spinach, cooked kale, raw spinach, raw parsley, goji berries, asparagus, and eggs



**Magnesium**

Sprouted pumpkin seeds, hemp seeds, chia seeds, Gerolsteiner mineral water, spinach, wild salmon, and peanut butter



**Manganese**

Mussels, wild blueberries, hazelnuts, pecans, oysters, clams, hummus, spinach, and cultivated blueberries



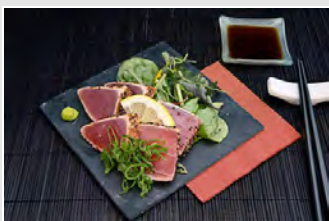
**Prebiotics**

Pistachios, leeks, asparagus, radicchio, bananas, garlic, kiwi, onions, artichokes, Tiger nuts, chicory root, yacon syrup and foods high in polyphenols



**Resveratrol**

Red grapes, peanut butter, Itadori tea, and dark chocolate



**Selenium**

Oysters, pork chops, beef, chicken breast, shrimp, eggs, shiitake mushrooms, and whole grain sourdough bread



**Vitamin A**

Liver, pastured eggs, cod liver oil, wild salmon oil, eel, and sockeye salmon



**Vitamin C**

Bell peppers, guava, black currants, strawberries, oranges, and broccoli



**Vitamin D**

Sockeye salmon, cod liver oil, canned tuna, wild herring, and sardines



**Zinc**

Oysters, crab, lobster, beef, lamb, pork loin, liver, and sprouted pumpkin seeds



# 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.



## B12

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



## B6

B6 levels may need to be tested



## Homocysteine

Homocysteine should be between 7-9



## Vitamin D

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



# MY CLINICAL RESEARCH SUMMARY

## 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-CYP2C19

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP2C19*17 rs12248560	Homozygous TT

### Recap

 Improves CYP2C19 Gene Function: Unknown.

 Decreases CYP2C19 Gene Function: Talk with your doctor regarding natural supplements and pharmaceutical drug interactions that may use this shared pathway.

## ESTROGEN METABOLISM-CYP2C19

Individuals with TT genotype for CYP2C19\*17 are considered the ultra-rapid metabolizer phenotype.

Women with CYP2C19\*17 T allele were associated with a decreased risk of breast cancer due to the increased metabolism of estrogen, thereby decreasing the level of harmful estrogen metabolites. The CYP2C19\*17 T allele decreased the risk of breast cancer in patients using hormone therapy.


Women with CYP2C19\*17 T allele were also associated with decreased risk of endometriosis.


## Estrogen Metabolism-CYP1A2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP1A2 rs762551	Homozygous AA

### Recap

 Improves CYP1A2 Gene Function: Unfiltered fermented drinks (Kombucha, beer, wine), hops, marinades, cruciferous vegetables, blueberries, blackberries, red grapes, kiwi, watermelon, parsley, and spinach.

 Decreases CYP1A2 Gene Function: Heterocyclic amines, nitrosamines, aflatoxin B1, polycyclic aromatic hydrocarbons, dioxins, and l-naphthoflavone. Omeprazole and primaquine are inducers. Caffeine and Tylenol combined with these compounds can make the effect worse.

## ESTROGEN METABOLISM-CYP1A2

CYP1A2 is a key enzyme in caffeine metabolism and the 2-hydroxylation of the main estrogens, estrone, and estradiol. 2-hydroxylation and 16 $\alpha$ -hydroxylation are two mutually exclusive pathways in estrogen metabolism. 2-hydroxyestrone acts as a weak estrogen or anti-estrogen. 16 $\beta$ -OHE1 acts as a procarcinogen.

Coffee may protect against breast cancer by altering estrogen metabolism. Women with higher coffee intake and the CYP1A2 homozygous AA fast metabolizer genotype have a ratio of high 2-hydroxyestrone to low 16 $\beta$ -OHE1. Researchers found that higher coffee intake was more protective against ER-positive breast cancer.

In men, a 2019 study found that low to moderate coffee intake and the AA fast caffeine metabolizer genotype were less likely to experience prostate grade cancer progression than non-consumers. In a large, pooled cohort of men with prostate cancer, coffee intake of more than 2.5 cups per day was associated with longer survival with the AA fast metabolizer genotype.

## Estrogen Metabolism-COMT

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
COMT rs4680	Heterozygous AG

### 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.

## ESTROGEN METABOLISM-COMT

COMT is a phase II enzyme involved in the inactivation of catechol estrogens that can otherwise lead to cancerous growth, while also increasing 2-methoxyestradiol, a metabolite that has been shown to inhibit the growth of breast cancer cells.

Variants in COMT V158M have been shown to decrease enzymatic activity and consequently increases the risk of carcinogenesis due to the accumulation of estrogen metabolites. COMT has been extensively investigated for correlation with different cancer risks including esophageal cancer, colorectal cancer, hepatocellular carcinoma, lung cancer, breast cancer, ovarian cancer, endometrial cancer, testicular germ cell tumor, and bladder cancer with mixed results.

Due to the COMT V158M heterozygous and homozygous genotypes potentially having reduced estrogen clearance, slowing this pathway down further with chronic stress and a high catecholamine intake combined with poor gut health and low magnesium intake may affect the level of harmful estrogen metabolites.

However, this doesn't mean catecholamines should be avoided. It simply means that the dosage should be altered. For example, green tea has been found to be beneficial for breast cancer prevention in the COMT heterozygous and homozygous genotype because these individuals retained the polyphenols the longest. The wild type may need more to achieve the same benefit. Less is more for COMT variants.

## MTNR1B-Melatonin

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
MTNR1B rs10830963	Heterozygous CG

### Recap



Late breakfast, early dinner, and avoiding late night snacking.



Oral contraceptives, night shifts, obesity, high-fat diet, and melatonin supplementation.

## MTNR1B-MELATONIN

**Research:** Melatonin is a hormone that helps to maintain our circadian rhythm such as the sleep-wake cycle, neuroendocrine rhythms or body temperature cycles through its action on melatonin receptors. The physiological effects of melatonin are various and include detoxification of free radicals and antioxidant actions, the activation of brown adipose tissue, bone formation and protection, reproduction, and cardiovascular, immune and body mass regulation. However, melatonin also affects glucose levels and insulin release.

In humans, melatonin release starts soon after sundown, reaches a peak between 2am and 4am and decreases gradually after that. However, in approximately one-third of individuals, there is a delay in melatonin release and stays elevated longer in the morning.

Dim light melatonin onset is defined as the start of the melatonin production in the evening during dim light conditions and has become a reliable phase marker of the circadian clock. One study found that MTNR1B rs10830963 G allele carriers had a significant association with delayed circadian phase of dim-light melatonin offset (1.37 hours) and a substantially longer duration of elevated melatonin levels in the morning (41 minutes).

MTNR1B rs10830963 has been associated with one of the strongest effects on insulin secretion and insulin sensitivity out of over 90 common variants identified for Type 2 diabetes and has been associated with gestational diabetes. Variants increase the amount of MTNR1B protein on the surface of insulin-producing cells, making the cells more sensitive to the effects of melatonin, which results in less insulin. Subjects carrying one or two G alleles showed a 2 to 4-fold increase in MTNR1B mRNA expression in human pancreatic islets, respectively, compared with the non-carriers.

The individuals with G allele of rs10830963 have been associated with increased plasma glucose level, decreased serum insulin level and an increased risk of Type 2 diabetes in Caucasians, Asians, African Americans and Hispanics. The researchers suggest that an increase of food intake to coincide with elevated melatonin levels in the evening and early morning lead to decreased glucose tolerance.

In a randomized, cross-over trial to compare glucose tolerance in the presence (late dinner 1 hour before bedtime) or absence (early dinner, 4 hours before bedtime) of elevated physiological melatonin concentrations, researchers compared the results between homozygous carriers and non-carriers of the MTNR1B risk allele. The concurrence of meal timing with elevated endogenous melatonin concentrations resulted in impaired glucose tolerance. This effect was stronger in MTNR1B risk-carriers than in non-carriers. Furthermore, eating late significantly impaired glucose tolerance only in risk-carriers and not in the non-risk carriers.

Results have also found that in carriers of the MTNR1B risk variant, melatonin supplementation (5 mg) significantly impaired glucose tolerance, with no effect in non-carriers. These results have been recently replicated, and are consistent with our findings even after chronic melatonin administration.

Oral contraceptives have been found to increase nighttime melatonin levels due to inhibiting catalyzing enzymes in the liver, and therefore could theoretically create a higher impact on insulin release and glucose tolerance in G carriers.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>SHBG</b></p> <p>Sex Hormone Binding Globulin (SHBG) is synthesized in the liver, and in the blood it transports and regulates the access of sex steroids to their target tissues.</p>	SHBG-rs1799941	GG		
	SHBG-rs12150660	GG		
<p><b>SHBG</b></p> <p>Sex Hormone Binding Globulin (SHBG) is synthesized in the liver, and in the blood it transports and regulates the access of sex steroids to their target tissues. Variants in this gene have been shown to lead to lower testosterone, calculated free testosterone and SHBG in men.</p>	SHBG-rs6258	CC		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>DI01</b></p> <p>DI01 is connected to thyroid health and is responsible for the deiodination of T4 into T3.</p>	DI01-rs2235544		AC	
<p><b>DI02</b></p> <p>DI02 is connected to thyroid health and is responsible for the deiodination of T4 into T3. D2 is the only activating deiodinase in the brain.</p>	DI02-rs225014	TT		
<p><b>CYP2R1</b></p> <p>Vitamin D is technically a hormone, and CYP2R1 is connected to circulating vitamin D levels.</p>	CYP2R1-rs10741657			GG
<p><b>CYP1A1</b></p> <p>CYP1A1 is in the estrogen metabolism pathway along with CYP1B1, CYP1A2, CYP3A1, SULT's and COMT.</p>	CYP1A1-rs1048943	TT		
<p><b>CYP2C19*17</b></p> <p>Genetic variability impacts expression and activity of CYP2C19 and therefore can influence drug metabolism and catabolism of estrogens.</p>	CYP2C19*17-rs12248560			TT
<p><b>CYP1A2</b></p> <p>CYP1A2 is a key enzyme in caffeine metabolism and the 2-hydroxylation of the main estrogens, estrone, and estradiol.</p>	CYP1A2-rs762551			AA
<p><b>COMT</b></p> <p>COMT is involved in catecholamine, dopamine, adrenaline, and estrogen metabolism through the inactivation of the catechol estrogens.</p>	COMT-rs4680		AG	
<p><b>FUT2</b></p> <p>The FUT2 gene controls prebiotic production, B12 absorption, and how much bifidobacteria you carry in your digestive tract.</p>	FUT2-rs601338		AG	

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>MTNR1B</b> The MTNR1B gene encodes for the melatonin receptor 1B.</p>	<p>MTNR1B- rs10830963</p>		<p>CG</p>	


# MACRONUTRIENT METABOLISM


## Beta Carotene to Vitamin A Conversion Rate-BCMO1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
BCMO1 R267S rs12934922	Homozygous TT
BCMO1 A379V rs7501331	Wild Type CC

### Recap

 Improves BCMO1 Gene Function: Vitamin A in the form of retinol and zinc.

 Decreases BCMO1 Gene Function: Relying on beta-carotene for vitamin A requirements.

## BETA CAROTENE TO VITAMIN A CONVERSION RATE-BCMO1

**Research:** If you are heterozygous or homozygous for BCMO1 A379V or BCMO1 RS267S, you have a reduced conversion of beta-carotene to vitamin A. If you have a heterozygous or homozygous BCMO1 RS267S and BCMO1 RS267S, the reduction is even more dramatic. Many nutrition labels will have beta-carotene listed as vitamin A, however this is not true vitamin A.

The normal conversion for beta-carotene (carrots, sweet potatoes) to retinol is 1:6 and 1:12 for other carotenoids. Female volunteers carrying the T variant of rs7501331 (379V) had a 32% lower ability to convert beta-carotene, and those carrying at least one T in both SNPs (379V and R267S) show a 69% lower ability to convert beta-carotene into retinol.

In a cohort study of 48,400 US men and 75,170 US women, during a follow-up period of more than 26 years, a higher total vitamin A intake was associated with a reduction in cutaneous squamous cell carcinoma risk.


You want to make sure you consume animal based vitamin A (pastured egg yolks, wild salmon oil, cod liver oil, butter) along with zinc for digestive lining repair, oral health, eye health, iron mobilization, mitochondria health, skin health (sunburns deplete vitamin A in the skin, and acne responds to vitamin A), healthy lung function, and increased immunity.


## B6-NBPF3

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
NBPF3 rs4654748	Homozygous CC

### 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.

**Research:** You may require a higher intake of B6. Homozygotes (CC genotype) have approximately a 2.90 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.

### Ghrelin and Appetite-FTO


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
FTO rs9939609	Homozygous AA
FTO rs17817449	Homozygous GG

#### Recap



Improves FTO Gene Function: A protein and fiber-rich breakfast, 7-8 hours of sleep per night, healthy vitamin D levels, and aerobic exercise over 1 hour or high-intensity exercise.



Decreases FTO Gene Function: Poor sleep patterns, refined carbohydrate breakfast, high saturated fat and low polyunsaturated fat intake, low vitamin D levels, and a sedentary lifestyle.

### GHRELIN AND APPETITE-FTO

**Research:** The FTO gene is highly expressed in the brain regions controlling feeding and energy expenditure, and is one of many genes associated with being a risk factor for obesity, especially abdominal weight. Polymorphisms in the FTO gene have been shown to cause higher ghrelin levels in many populations, which can create a larger appetite and the potential for overeating.

FTO encodes for an enzyme able to remove methyl groups from DNA and RNA, and the FTO polymorphisms may reduce the methylation of ghrelin (hunger hormone), leading to higher ghrelin levels and potentially affecting other genes. Although rs9939609 has been replicated across a number of cohort studies for obesity, there remains significant variance due to epigenetic expression.

Studies have proposed that FTO alters dopamine signaling, affecting reward brain structures. This may be especially true for those who also have variants in ANKK1, the gene for dopamine receptor density. Research has shown that in cases of reduced D2 receptor availability, as indicated by the ANKK1 polymorphism, FTO variants were associated with increased body fat, waist circumference and reduced peripheral insulin sensitivity. This could increase the risk of obesity and Type 2 diabetes.

This may explain why the FTO rs9939609 homozygous genotype preferentially selects high calorie/high-fat food compared to the normal TT genotype. Multiple studies have shown that a high dietary saturated fat intake (higher than 15.5% energy) and a low dietary polyunsaturated fat intake further increased the risk of being overweight or abdominally obese for the AA genotype. The non-risk TT allele carriers appeared to be unresponsive to dietary saturated fat intake or the dietary polyunsaturated to saturated fat intake ratio in regards to obesity.

Ghrelin is highest in the fasting state, before meals, and at night, falling within one hour of a meal. Research has found that a breakfast centered around protein and fiber-rich carbohydrates (especially prebiotic fiber) was the most effective at suppressing ghrelin levels throughout the day, while also focusing on polyunsaturated and monounsaturated fats.

In a single-blind crossover study, three high fat meals (70% of energy) rich in monounsaturated (MUFA), polyunsaturated (PUFA) or saturated fat (SFA) in 16 women with obesity were tested. A decrease in ghrelin was significantly greater for PUFA and MUFA vs. SFA while appetite suppression was significantly greater for PUFA vs. both SFA and MUFA. One study also found that subjects with vitamin D levels of less than 20ng/ml had significantly higher ghrelin levels than those with a vitamin D level greater than 20/ml.

People with the homozygous FTO genotypes may be more prone to overeating when eating a high-saturated fat meal or purely refined carbohydrate breakfast and getting poor sleep due to higher ghrelin levels. One study found that a reduction of sleep duration to 4-hours for two consecutive nights was shown to decrease circulating leptin levels and increase ghrelin levels, as well as self-reported hunger.

The key to improving FTO gene function is through lowering ghrelin levels, and those with the homozygous genotypes may gain the most significant benefits from preventative and treatment strategies aimed at targeting the ghrelin system and modulating reward responsiveness. The ANKK1 gene for dopamine receptors is also a relevant gene for appetite control and should be reviewed as well.

Regarding exercise, research has shown that doing 120 min prolonged treadmill exercise with mix intensity or high-intensity exercise was the most effective at suppressing ghrelin, while weight training or low-intensity exercise did not have the same effects. If weight loss and appetite suppression is your goal, aerobic exercise with a mixture of high intensity may be the best approach.


We recommend reviewing ANKK1, PPAR-alpha, ACSL1, APOA2, ADIPOQ, SLC22A5, FUT2 and CYP2R1 if your goal is weight loss and you want to further assess your saturated fat metabolism.

## Carbohydrates-TCF7L2


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
TCF7L2 rs7903146	Heterozygous CT

### Recap



Improves TCF7L2 Gene Function: A Paleolithic and low-carb Mediterranean diet, glycine, omega-3 fatty acids, olive oil, turmeric, cinnamon, prebiotics, organic dark roast coffee, and cordyceps mushrooms.



Decreases TCF7L2 Gene Function: Refined sugar and grains.

## CARBOHYDRATES-TCF7L2

**Research:** The TCF7L2 gene has become the strongest indicator of Type 2 diabetes and gestational diabetes risk for multiple ethnicities in studies. A meta-analysis also found an association with breast, prostate and colon cancer risk, all of which are connected to blood sugar levels and the risk is reduced by many of the same nutrients that improve this gene's function. Other genes and family history need to be assessed for cancer risk and prevention.

This gene is unique in its relation to Type 2 diabetes because people with variants in TCF7L2 may not exhibit risk signs like obesity. In fact, they may have a low body mass index (BMI) and low triglycerides. The increased risk is hypothesized to be due to the effect of TCF7L2 on the sensitivity of the pancreatic  $\beta$ -cells to incretins, not overall insulin sensitivity.

Incretins are hormones that are released from the gastrointestinal tract after a meal and regulate the amount of insulin secreted. The two most important incretin hormones are GLP-1 and GIP. Researchers believe that increasing incretin sensitivity may decrease the risk of type 2 diabetes.



rich foods, fiber-rich vegetables, and spices high in phytochemicals resulted in significant increases in incretin and increased perceived satiety (feeling full). All three test meals were normalized to contain 50 grams of carbohydrates. Sufficient protein in particular shows promise in the management of Type 2 diabetes by stimulating incretin, insulin secretion, and slowing gastric emptying.

Two clinical studies have demonstrated that plasma GLP-1 levels rise following the ingestion of gelatin, a protein extraordinarily rich in glycine. Another study found that higher levels of indolepropionic acid produced by good bacteria due to a diet higher in prebiotic fiber-rich food decreased the risk of Type 2 diabetes.

Spices also appear very effective. Turmeric significantly increases the secretion of the incretin GLP-1. Cinnamon lowers blood glucose usually within physiological levels without hypoglycemia and increases satiety, showing it may act by potentiating the effects of incretin hormones.


There is a progressive deterioration of beta-cell function in patients with Type 2 diabetes. In vitro studies demonstrated that pancreatic beta-cell viability increased dramatically with cordyceps extract treatment, implying that cordyceps protect beta cells. This is crucial for the TCF7L2 gene due to the communication between pancreatic beta cells and incretins. The researchers concluded that "the potential ability of cordyceps to preserve beta-cell function may afford a promising therapy for diabetes."

### Stress and IBS-ADRB2


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ADRB2 rs1042714	Heterozygous CG

### Recap



Increases ADRB2 Gene Function: Deep breathing techniques, meditation, yoga, magnesium, and vitamin C.



Decreases ADRB2 Gene Function: Chronic stress and shallow breathing.

### STRESS AND IBS-ADRB2

The pathogenesis of digestive disorders is incompletely understood, although genetic factors, low-grade inflammation, intestinal dysbiosis, abdominal pain, and brain-gut axis dysfunction all have been postulated to contribute.

The beta-2-adrenergic receptor (ADRB2) is the main target of the catecholamine epinephrine and a primary mediator of the stress response. ADRB2 is widely expressed both in the gastrointestinal tract and in the CNS.

Single-nucleotide polymorphisms (SNPs) located in the coding region of the ADRB2 gene have been shown to be associated with increased altered receptor response to catecholamines as well as altered receptor expression. In the case of rs1042714, this may lead to decreased receptor degradation and down-regulation, in turn enhancing the adrenaline response.

For the rs1042714 genotype, both GG homozygotes and CG heterozygotes demonstrated a higher percentage of digestive issues compared with CC homozygotes. The G allele carriers were associated with a higher percentage of IBS cases, twice the rates of anxiety, and functional chest pain diagnoses. Within IBS, G allele carriers had more severe bowel symptoms and symptomatic days.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
HLA DQ2.5	HLA DQ2.5- rs2187668		CT	

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<b>HLA-DQ8</b>	HLA-DQ8- rs7454108	TT		
<b>BCMO1 R267S</b> BCMO1 encodes the conversion rate from beta-carotene to vitamin A.	BCMO1 R267S- rs12934922			TT
	BCMO1 A379V- rs7501331	CC		
<b>FADS2</b> The FADS2 gene encodes the conversion of plant based omega-3 fatty acid alpha linolenic acid (ALA) to EPA.	FADS2-rs1535	AA		
	FADS2-rs174575	CC		
<b>FUT2</b> The FUT2 gene controls prebiotic production, B12 absorption and how much bifidobacteria you carry in your digestive tract. The rs601338 SNP is found in European, African and Indian populations.	FUT2-rs601338		AG	
<b>NBPF3</b> NBPF3 has been associated with vitamin B6 levels.	NBPF3-rs4654748			CC
<b>SLC23A1</b> Solute carrier family 23 member 1 (SLC23A1) is one of the two transporters which aids in the absorption of vitamin C into the body. Polymorphisms in the gene are associated with reduced plasma vitamin C levels in the body.	SLC23A1- rs33972313	CC		
<b>ACAT1-02</b> The ACAT gene converts protein and fat to ATP (energy) in the mitochondria, and plays an important role in cellular cholesterol homeostasis.	ACAT1-02- rs3741049	GG		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>ADIPOQ</b></p> <p>ADIPOQ encodes for adiponectin, a protein secreted by fat cells that affect insulin and glucose metabolism. Low levels of adiponectin play a role in obesity, insulin resistance and Type 2 diabetes.</p>	ADIPOQ-rs2241766	TT		
<p><b>HFE-C282Y</b></p> <p>A homozygous HFE C282Y may lead to an iron overload due to increased iron absorption and disrupted metabolism.</p>	HFE-C282Y-rs1800562	GG		
<p><b>HFE-C282Y</b></p> <p>A heterozygous HFE C282Y and HFE H63D gene may lead to an iron overload due to increased iron absorption and disrupted metabolism.</p>	HFE-C282Y-rs1800562	GG		
<p><b>PPAR-alpha</b></p> <p>The PPAR-alpha gene plays a vital role in fatty acid metabolism and ketosis, and is considered one of the most critical targets for ameliorating abnormalities with triglycerides, HDL, LDL, VLDL, and ApoB.</p>	PPAR-alpha-rs1800206	CC		
<p><b>ACSL1</b></p> <p>Long-chain acyl CoA synthetase 1 (ACSL1) plays an important role in fatty acid metabolism and triglyceride synthesis. Disturbance of these pathways may result in dyslipidemia and insulin resistance, hallmarks of the metabolic syndrome.</p>	ACSL1-rs9997745			AA
<p><b>FTO</b></p> <p>Polymorphisms in the FTO genes have been shown to cause higher ghrelin levels (hunger hormone) in many populations, which can create a larger appetite and the potential for overeating.</p>	FTO-rs9939609			AA
	FTO-rs17817449			GG

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>APOA2</b></p> <p>The APOA2 gene contains instructions for making a protein called apolipoprotein A-II, which is found in HDL cholesterol particles. The homozygous genotype has been linked to saturated fat intake and weight gain.</p>	APOA2-rs5082	AA		
<p><b>TCF7L2</b></p> <p>TCF7L2 polymorphisms have been associated with low incretin hormones and impaired insulin secretion.</p>	TCF7L2-rs7903146		CT	
<p><b>LCT</b></p> <p>LCT is the gene connected with the ability to breakdown lactose in dairy.</p>	LCT-rs4988235		AG	
<p><b>APB1</b></p> <p>APB1 encodes for the DAO enzyme to breakdown histamines primarily in the digestive tract. The homozygous genotype may increase the risk of migraines from histamines in women or a hypersensitivity to Aspirin in men.</p>	APB1-rs10156191	CC		
<p><b>ABCG2 (Q141K)</b></p> <p>The ABCG2 (Q141K) gene is located at the membrane of kidney proximal tubule cells, where it mediates renal urate secretion. Variants in this gene are linked to reduced uric acid excretion.</p>	ABCG2 (Q141K)-rs2231142	GG		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>ALDH2</b></p> <p>Alcohol metabolism in the liver most commonly involves the enzymes alcohol dehydrogenase and aldehyde dehydrogenase, metabolizing alcohol to acetaldehyde, and then to acetate. ALDH2 encodes for aldehyde dehydrogenase, and variants can affect the levels of acetaldehyde and therefore the carcinogenic effect of alcohol.</p>	ALDH2-rs671	GG		
<p><b>ADRB2</b></p> <p>The beta-2-adrenergic receptor (ADRB2) is the main target of the catecholamine epinephrine, and a primary mediator of the stress response. ADRB2 is widely expressed both in the gastrointestinal tract and in the CNS.</p>	ADRB2-rs1042714		CG	
<p><b>PPCDC</b></p> <p>PPCDC is necessary for the biosynthesis of coenzyme A and variants in this SNP are associated with serum zinc levels.</p>	PPCDC-rs2120019		CT	
<p><b>SELENBP1</b></p> <p>The Protein Selenium Binding 1 gene codes for an integral membrane protein involved in antigen presentation and serum copper levels.</p>	SELENBP1-rs2769264	TT		
<p><b>TFR2</b></p> <p>The TFR2 gene provides instructions for making a protein called transferrin receptor 2 to help iron enter liver cells. The receptor on the surface of liver cells binds to transferrin, which transports iron through the blood to tissues throughout the body. When transferrin binds to transferrin receptor 2, iron is allowed to enter the cell.</p>	TFR2-rs7385804			CC

# 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.

## Cell Protection-CAT

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CAT C-262T rs1001179	Heterozygous CT

## Recap



Improves CAT Gene Function: Black cumin seed oil, ginger, Lion's Mane, flavonoids, healthy iron levels, selenium, boron, cumin, anise, fennel, caraway, cardamom, lutein, holy basil and deep breathing relaxation techniques.



Decreases CAT Gene Function: Oxidative stress and BPA plastic.

## CELL PROTECTION-CAT

**Research:** CAT makes an enzyme called catalase, which helps reduce oxidative stress. CAT is present in all aerobic cells while research has found the highest correlation to prostate, breast, liver and blood health.

There are several SNPs identified in the CAT gene, of which the rs1001179 polymorphism (C262T) is the most extensively studied. In comparison with the variant C allele, the variant T allele of the CAT C262T polymorphism has been reported to indicate lower CAT enzymatic activity, higher sensitivity to oxidative stress, and increased DNA damage risk, which can lead to cancer.

If you have variants in CAT C26T, you may have a higher need for flavonoids, selenium, ginger, cumin, anise, fennel, caraway, cardamom, watching iron levels, and deep breathing relaxation techniques (yoga, meditation, prayer) to assist catalase.

Ginger consumption has been reported to decrease lipid peroxidation and normalize the activities of superoxide dismutase and catalase, as well as GSH and glutathione peroxidase, glutathione reductase, and glutathione-S transferase.

Lion's Mane has been found to promote ulcer protection and significant protection activity against gastric mucosal injury by preventing the depletion of antioxidant enzymes. Treatment with a hot water extract of Lion's Mane decreased lipid peroxidation and increased superoxide dismutase (SOD) and catalase (CAT) activities, quenching free radicals in the gastric tissue of ethanol-induced rats to exhibit gastroprotective activity.

## 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-GPX1


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
GPX1 rs1050450	Homozygous AA

### Recap



Improves GPX1 Gene Function: Selenium, optimal testosterone and estradiol levels, melatonin, vitamin C, vitamin E, black cumin seed oil, flavonoids, milk thistle, ginger, cumin, anise, fennel, caraway, cardamom and cryotherapy.



Decreases GPX1 Gene Function: Selenium deficiency, statin drugs, iron deficiency or elevated iron, and lead.

## GLUTATHIONE-GPX1

**Research:** Superoxide dismutase (SOD) transforms the inflammatory superoxide to hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), and the next step is for glutathione peroxidase (GPX1) to transform it to water (H<sub>2</sub>O). When GPX1 function is modulated by polymorphisms and other factors affecting its function, a hydroxyl radical may be more likely to form which attacks DNA and causes strand breaks.

Research has shown that there is reason to believe that individual requirements for selenium will differ because of polymorphisms in seleno-protein genes. In a study looking at a New Zealand population, homozygous minor allele carriers of GPX1 rs1050450 had lower GPX1 activity than other genotypes with the same selenium status.



Elevated lead levels may have more toxic effects with GPX1 polymorphisms. A study looking at 362 patients and 494 controls found that lead exposure and GPX1 polymorphisms were significantly associated with glioblastoma and meningioma. Vitamin C decreases blood lead levels, and calcium reduces lead uptake.

GPX1 activity is considered to be the most important antioxidant enzyme defense mechanism in the skin. In a study from the Journal of Dermatological Science, the homozygous genotype for GPX1 rs1050450 was associated with a two-fold increased risk of melanoma.

Statins inhibit the biosynthesis of selenium-containing proteins, one of which is glutathione peroxidase serving to suppress peroxidative stress. An impairment of selenoprotein biosynthesis may be a factor in congestive heart failure, reminiscent of the dilated cardiomyopathies seen with selenium deficiency. A meta-analysis found that East Asian populations may be prone to cardiovascular issues with GPX1 polymorphisms.

Oxidative stress and inflammation play a pivotal role in the pathogenesis of Hashimoto's disease, an autoimmune disorder. A study looking at patients in Northwest Iran found that antioxidant capacity in Hashimoto's patients was lower than healthy controls. There was also a significant association with variants in GPX1 rs1050450, elevated anti-TPO levels, and Hashimoto's risk. The thyroid is the organ with the highest amount of selenium per gram of tissue. Research has suggested that selenium supplementation of patients with Hashimoto's disease is associated with a reduction in anti-TPO levels, improved thyroid ultrasound features, and improved quality of life.

In an experiment investigating the effect of heat and cold stress on glutathione metabolism in human erythrocytes, men were immersed at three different water temperatures for 10 min. At 39 degrees C (102 F), glutathione peroxidase decreased from 35.90 (1.83) to 34.33 (1.66) IU.g. The researchers concluded that "these changes indicate that heat stress causes oxidative stress in the human body; however, cold stress is thought to augment the activity of the antioxidative defense system. It is suggested that body exposure to hot environmental conditions should not be recommended for patients suffering from a damaged antioxidative defense system."


One study found that elite kayakers that engaged in whole body cryotherapy (-248 to 284°F or -120 to 140°C) for 3 minutes a day for 10 days increased the activity of superoxide dismutase by 36% and glutathione peroxidase by 68%.

## Eye Health-CFH


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CFH rs1061170	Homozygous CC

## Recap



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



Decreases CFH 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-CFH

**Research:** Age related macular degeneration (AMD) is the leading cause of blindness in Western societies, but its etiology remains largely unknown.

Variants in CFH confers a 2-fold higher risk of late AMD per copy in individuals of European descent. Research indicates that CFH (rs1061170) polymorphism impacts significantly on retinal function in early AMD patients, and supports the hypothesis that a dysfunctional CFH might result in early retinal function loss due to a reduction in the immune antioxidant defense mechanism. A study from 2005 found that variants in CFH likely explains approximately 43% of AMD in older adults.

Malondialdehyde (MDA) is a common lipid peroxidation product that accumulates in many pathophysiological processes, including AMD. In vivo studies in mice found CFH as a major MDA-binding protein that blocks MDA-modified proteins by macrophages and MDA-induced pro-inflammatory effects. The CFH polymorphism markedly reduces the ability of CFH to bind

MDA, indicating a causal link to a cause of age related macular degeneration.

A recent meta-analysis found that the rates of myopia (nearsightedness) will increase 140% by 2050 due to our increased time in front of a screen. Myopia can increase the risk of numerous eye disorders. Blue light is a high-energy or short-wavelength visible light from your phone and computer that induces inflammation and retinal diseases such as age-related macular degeneration and retinitis pigmentosa. Research has found that bilberry and lingonberry exert protective effects against blue LED light-induced retinal photoreceptor cell damage due to their polyphenol content.

Lutein and zeaxanthin can inhibit oxidation of cell membranes and may be protective against UV-induced eye damage. Studies have demonstrated that people in the highest quintile of intake of dietary carotenoids, especially lutein and zeaxanthin concentrations have significantly lower risk of macular degeneration. Blue-eyed adults have far less lutein and zeaxanthin in their retinas.

One study compared diets of 356 patients with macular degeneration with 520 patients with other eye diseases. The data revealed that beta carotene was not especially effective, but that lutein and zeaxanthin were. Another study found that the risk of macular degeneration was reduced 65 percent with high amounts of lutein and zeaxanthin.

Research has found that MDA levels are significantly increased in groups of subjects with deficient levels of vitamin C and vitamin E. Deficiency in these two antioxidants leads to insufficient defense against free radicals and increased MDA levels. Those with polymorphisms in CTH should increase vitamin C and vitamin E intake. In another study, the risk for macular degeneration was found to be 77% lower when vitamin C supplements and a low-glycemic diet was used.

One study followed 3,600 people ages 55-80 years old for six years and found that those that took antioxidants plus zinc were less likely than those who took only antioxidants or only zinc to lose their vision.


Studies show that people who consume more fish, which is rich in DHA-fish fat, are less likely to develop macular degeneration. Eating fish one to three times a week has been associated with a 40 to 75 percent reduction in macular degeneration.


## COVID 19 Severity-LZTFL1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
LZTFL1 rs17713054	Homozygous AA

### Recap

 Currently unknown.

 Currently unknown.

## COVID 19 SEVERITY-LZTFL1

**Research:** The LZTFL1 gene influences the transition of specialized lung cells to less specialized lung cells during infection and inflammation. Low levels of LZTFL1 promote this transition, while high levels slow the transition. The hypothesis is that less specialized lung cells have fewer ACE2 receptors, and therefore, less chances for viral entry from SARS-CoV-2.

Scientists found that the LZTFL1 gene high-risk variant affects the lungs, but does not have an impact on the immune system. People with the variant genotype have higher levels of LZTFL1, slowing the transition to less specialized cells, leaving more specialized lung cells vulnerable to SARS-CoV-2 viral entry, replication and severity.

Scientists at the University of Oxford published results in November 2021 that variants in the LZTFL1 gene doubled the risk of lung failure and death from COVID-19. Approximately 60% of people with South Asian ancestry, 15% of people with European ancestry, 2% of people with African-Caribbean ancestry and 1.8% of people with East Asian ancestry carry the high-risk variant.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>SOD2</b></p> <p>Superoxide dismutase (SOD2) is manganese dependent and protects against superoxide for the mitochondria of the cell. Variants here increase the need for intracellular antioxidant protection.</p>	SOD2-rs4880		AG	
<p><b>SOD3</b></p> <p>Superoxide dismutase (SOD3) is zinc/copper dependent and protects against superoxide for the cell membrane. Variants here increase the need for intracellular and extracellular antioxidant protection.</p>	SOD3-rs1799895	CC		
<p><b>CAT C-262T</b></p> <p>CAT makes an enzyme called catalase, which helps reduce oxidative stress.</p>	CAT C-262T-rs1001179		CT	
<p><b>GSTM1</b></p> <p>GSTM1 catalyzes the detoxification of alkyl and polycyclic aromatic hydrocarbons (PAHs), intermediate forms of many carcinogens, specifically metabolically generated epoxide intermediates of benzo(a)pyrene.</p>	GSTM1-rs366631	AA		
<p><b>GSTP1 I105V</b></p> <p>Glutathione S-Transferase (GSTP1) is linked to the metabolism of mutagens, carcinogens, and other poisonous chemicals. It plays a crucial role in the detoxification process, thereby protecting cells from these compounds. GSTP1 rs1695 is connected to breast, prostate, urinary, esophagus, and skin health.</p>	GSTP1 I105V-rs1695	AA		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>GSTP1 C341T</b></p> <p>Glutathione S-Transferase (GSTP1) is linked to the metabolism of mutagens, carcinogens, and other poisonous chemicals. It plays a crucial role in the detoxification process, thereby protecting cells from these compounds. GSTP1 rs1138272 is connected to the colon, prostate, lung, throat, and fertility.</p>	GSTP1 C341T-rs1138272	CC		
<p><b>GPX1</b></p> <p>The GPX1 (Glutathione peroxidase 1) gene encodes a protein responsible for the modulation and detoxification of hydroperoxides and hydrogen peroxide to protect the mitochondria and cytoplasm of cells against oxidative damage.</p>	GPX1-rs1050450			AA
<p><b>CTH</b></p> <p>The CTH (Cystathionine Gamma-Lyase) gene encodes an enzyme in the trans-sulfuration pathway that converts cystathionine derived from methionine into cysteine. Glutathione synthesis in the liver is dependent upon the availability of cysteine.</p>	CTH-rs1021737	GG		
<p><b>NOS1</b></p> <p>NOS1 (nNOS) codes for brain neural transmission, memory, learning, psychological stress, the peripheral nervous system and potentially the lymph nodes.</p>	NOS1-rs3782218	CC		
<p><b>NOS2</b></p> <p>NOS2 (iNOS) encodes for wound, tissue damage, infection and hypoxia (low oxygen).</p>	NOS2-rs2248814		AG	

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>CFH</b></p> <p>CFH (complement factor H) polymorphism is associated with increased risk of age related macular degeneration.</p>	CFH-rs1061170			CC
<p><b>ARMS2</b></p> <p>ARMS2 polymorphism is associated with increased risk of age related macular degeneration (AMD).</p>	ARMS2-rs10490924	GG		
<p><b>LZTFL1</b></p> <p>The LZTFL1 gene influences the transition of specialized lung cells to less specialized lung cells during infection and inflammation.</p>	LZTFL1-rs17713054			AA


# 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.

## Dopamine, Adrenaline and Estrogen-COMT


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
COMT V158M rs4680	Heterozygous AG
COMT rs4633	Heterozygous CT

## 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.

Studies have found that the AG allele in COMT V158M (rs4680) results in an intermediate enzymatic function, while the wild type GG has fast activity, and the AA homozygous genotype has 4-5 times lower COMT activity. This means that dopamine and adrenaline levels should be more level in the AG genotype. However, multiple studies have shown that the AG genotype may fall on the higher end of the dopamine spectrum with cognitive tests.

Research has shown that individuals carrying the A allele of rs4680 or T allele of rs4633 scored significantly higher on insight problem-solving tasks, and for the COMT H62H rs4633 gene, the homozygous TT and heterozygous TC carriers had higher insight problem-solving scores than those with wild-type CC genotype.

A small study found 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.

There are both benefits and detrimental aspects to variants in COMT. The downside of the A allele in COMT V158 is that the body overreacts to stress and pressure that can lead to anxiety, depression, impulsiveness, obsessive behavior, irritability, ADHD and abnormal behavior. It can also create a sensitivity to a higher intake of catecholamines (coffee, black tea, green tea, red wine, chocolate), especially in a stressed state, leading to high dopamine and adrenaline levels making the stress response worse. However, green tea has been found to be beneficial for breast cancer prevention in the AG and AA genotype because these individuals retained the polyphenols the longest. Other genetic variants involved in dopamine transport and receptor function also influence this magnitude.

Having a heterozygous variant in COMT V158M may increase your need for magnesium, vitamin C, and healthy copper levels (not too high or low). Compound weight lifting (squats, bench press, deadlift), sprints, and chopping wood can assist a slow COMT enzyme by increasing testosterone levels, which speed up the pathway and lower the stress response. Supplementation of magnesium and vitamin C may be essential to modulate COMT due to low magnesium levels in the water and soil, or lack of freshly picked fruits and vegetables for vitamin C, and chronic stress levels.

## 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.


## Histamines and Migraines-HNMT


Below is a summary of your most significant variant genotypes:



GENE	GENOTYPE
HNMT C314T rs11558538	Heterozygous CT

## Recap

 Improves HNMT Gene Function: Vitamin C, choline, folate, magnesium, chamomile, basil, stinging nettle, echinacea, fennel, ginger and wild oregano.

 Decreases HNMT Gene Function: Poor gut flora, too many fermented foods, red wine, NSAID's, antidepressants, histamine H2 blockers, antihistamines, antiarrhythmics, immune modulators, deficiencies in vitamin C, choline, folate and magnesium.

## HISTAMINES AND MIGRAINES-HNMT


If you have also the GG genotype for DAO rs1049793, the co-presence of the T allele (TC or TT) in HNMT rs11558538 may increase the degree of disability of migraines from histamines. Further studies are needed to confirm the HNMT polymorphism connection to migraines.


## 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), ß-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 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.


## Brain Health-PEMT

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
PEMT rs7946	Heterozygous CT
PEMT rs12325817	Wild Type CC

## Recap

 Improves PEMT Gene Function: Choline, vitamin C, and estrogen.

 Decreases Gene Function: Nighttime pain relievers, antihistamines, sleep aids, antidepressants, incontinence drugs and narcotic pain relievers.

## BRAIN HEALTH-PEMT

**Research:** Choline is required for acetylcholine, a neurotransmitter of the vagus nerve that enervates multiple organs including the lungs, heart, liver, stomach, ovaries and temporal lobe of the brain. A deficiency could affect all of these, especially memory. Acetylcholine also plays a role in promoting REM sleep.

Having one or more T alleles at rs7946 is associated with having lower phosphatidylcholine production in the liver.

Eighty percent of the women who were homozygous for the rs12325817 SNP manifested signs of choline depletion (liver or muscle dysfunction), relative to 43% of subjects carrying one copy of the variant allele and 13% of subjects without the SNP.

Vitamin C has been shown to induce the release of acetylcholine from synaptic vesicles of neurons and increase acetylcholine levels in the brain.

Possible drugs that can cause memory loss include antidepressants, antihistamines, anti-anxiety medications, anti-seizure drugs, muscle relaxants, tranquilizers, sleeping pills, and pain medications given after surgery. Why? The majority of these are in a class called anticholinergic drugs and block acetylcholine.

A French study looking at 4,128 women and 2,784 men that reported taking anticholinergic drugs showed a greater decline over four years in verbal fluency scores and in global cognitive functioning than women not using anticholinergic drugs. In men, an association was found with a decline in visual memory and to a lesser extent in executive function. Significant interactions were observed in women between anticholinergic use and age, APOE genotype, or hormone replacement therapy. A significantly 1.4–2 fold higher risk of cognitive decline was observed for continuous anticholinergic users.

These drugs could be especially theoretically problematic for those with poor PEMT function, low estrogen (in women) and a family history of dementia and Alzheimer's disease.

Research shows that only 15% of women get enough choline, and one study found that those with lowest choline have the highest anxiety.

## Panic and PTSD-GAD1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
GAD1 rs3749034	Heterozygous AG

### Recap



Probiotics, B6, B2, taurine, magnesium, lithium, choline, vitamin C, zinc, vitamin D, progesterone (women), CBD, lemon balm, ashwagandha, high intensity exercise for 8-20 minutes, endurance exercise, yoga, meditation, and deep sleep.



Antibiotics, caffeine, high estrogen, excess wheat, excess sugar, broth cooked over 24 hours, low blood sugar, poor sleep, manganese deficiency, boron deficiency, chronic stress, proton pump inhibitors, diuretics, hormone replacement therapy, MAOI's, fibrates, MSG, low progesterone, sucralose and aspartame.

## PANIC AND PTSD-GAD1

GAD1 stands for "Glutamate Decarboxylase 1" and is responsible for the conversion of glutamate to GABA. GABA and glutamate account for 80% of brain activity. Glutamate is excitatory while GABA is calming. In the right amounts, glutamate helps focus, cognitive function and productivity. Too much, however, can be excitatory and detrimental.

The GAD system influences mood stability and the pathophysiology of mood and anxiety disorders. To date, GAD1 genetic variants have been associated with mood disturbance, and panic disorder. GAD1 SNPs may impact both mood and anxiety-like traits, and may also be relevant following stress or trauma exposure in influencing risk for PTSD as well as depression.

The subjects carrying A allele of rs3749034 were associated with an increased risk of Posttraumatic stress disorder when compared to subjects with the "G" allele in the dominant model.

GABA levels in various brain regions are reduced in panic patients possibly due to impaired GAD function. Further studies in patients with major depression found reduced GABA levels to be accompanied by increased glutamate concentrations strengthening the link between anxiety and mood disorders and GAD.

Following a trauma, individuals at higher genetic risk with certain genotypes in GAD1 may experience physiological effects of anxiety, overconsolidation of the fear memory, and negative thoughts about the event, decreasing their ability to extinguish fear responses when reminded of the trauma and increasing the likelihood of mood-related disturbances. Therefore the correlation with a genetic predisposition to a higher trauma response may require variants in GAD1, an environmental trauma, and gender to due the influence of estrogen on GAD.

Estrogen and progesterone decrease GAD expression in the amygdala and the hippocampus (which both are involved in regulating fear), which provides a link between hormone levels and anxiety as well as mood changes during menstruation in women. Natural progesterone in women (B6 helps produce progesterone) has powerful effects on enhancing GABA activity in the brain. When progesterone is too low, it causes elevated glutamate levels.

Abnormalities in the GABA neurotransmitter system have been noted in subjects with mood and anxiety disorders, which is why anticonvulsants are also marketed for mood disorders. Lithium and the drug Lamictal has been shown to help regulate the neurotransmitter glutamate by keeping the amount of glutamate between brain cells at a stable, healthy level. The anticonvulsant drug Topamax is used for migraines by lowering glutamate and raising GABA levels.

Excess glutamate is supposed to convert to GABA with B6 and magnesium. GAD1 variants slow down the conversion of glutamate to GABA and increase the need for B6/magnesium to make it run normally. Studies have found that exercise helps the brain direct excess glutamate to be used as an energy source and prevent toxic build-up.

GABA requires adequate probiotics (bifidobacterium produces large amounts of GABA, so the FUT2 gene function should also be assessed) zinc, B2, B6, vitamin C, vitamin D and deep sleep to keep glutamate in check. Taurine (found in grass-fed animal protein, wild fish and eggs) appears to increase the levels of GAD1 to reduce glutamate and help bind to GABA receptors in brain cells.

One study found that neuronal excitability from glutamate appears to be attenuated when eating or supplementing with the mushroom Lion's Mane. Research on Lion's Mane also shows that the hot water extract stimulates Nerve Growth Factor (part

of a family of similar proteins that serve to promote the health and normal function of the brain and nervous system) and accelerates the growth of the myelin sheath. This has exciting potential for those with neurodegenerative disorders from high glutamate levels.

The artificial sweetener aspartame is especially troubling for those with GABA and glutamate imbalances. The lowered levels of serotonin due to aspartame consumption might cause lowered activity of the GABA transporters.

## Glutamate Transport-SLC17A7

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
SLC17A7 rs74174284	Homozygous GG

### Recap



Improves SLC17A7 Gene Function: Zinc, omega-3 fatty acids (EPA and DHA), lion's mane mushroom, B6, lithium, magnesium, B2, folate, B12, vitamin C, melatonin, choline, vitamin D and exercise.



Decreases SLC17A7 Gene Function: Head injuries

## GLUTAMATE TRANSPORT-SLC17A7

**Research:** Polymorphisms in SLC17A7 are associated with delayed recovery time from head injuries. The hypothesis for this is that variants in this gene reduce glutamate transport, which leads to high concentrations of glutamate within the synaptic cleft after trauma.

Glutamate is the primary excitatory neurotransmitter in the brain, while GABA is the principal inhibitory (relaxing) neurotransmitter. Following a head injury, high glutamate release is responsible for excitotoxicity that leads to neuronal injury, mitochondrial dysfunction and dysfunction of surviving neurons. The loss of GABA producing cells disrupts the balance of excitation and inhibition leading to further cell injury. This glutamate toxicity seen in brain injuries is also the process shared in epilepsy and neurodegenerative disorders. Therefore, a goal should be to restore normal glutamate and GABA function for a head injury recovery protocol.

One study in 2016 took saliva samples from 40 athletes diagnosed with a sport-related concussion by a physician. An association was found between the normal genotype of SLC17A7 and recovery, where those carrying the minor G allele were 6.33-times more likely to experience prolonged recovery rates exceeding 20 days. Those carrying the GG genotype had worse motor speed scores upon initial assessment compared to both heterozygous (CG) and homozygous (CC) genotypes. Based upon these findings, rs74174284 is a potential predictive genetic marker for identifying athletes who are more susceptible for altered recovery times and worse motor speed scores after sport-related concussion.

The majority of traumatic brain injuries (TBI) cases can be attributed to motor vehicle accidents, motorcycle accidents, bicycle accidents, and pedestrian injuries. It is also a major concern in contact sports.

In football and hockey, the number of actual concussions is six or seven times higher than the number diagnosed. Approximately 70 percent of football players and 62 percent of soccer players get at least one concussion per year.

In a study of Norwegian soccer players, 81 percent had an impairment of attention, concentration, memory, and judgment ranging from mild to severe.

A study from the Archives of Pediatrics & Adolescent Medicine found that children who suffer concussions may experience lingering problems with memory and attention, even 12 months after the injury.

Human clinical data suggests that supplemental zinc can be used during recovery to improve cognitive and behavioral deficits associated with brain injury. Additionally, pre-clinical models suggest that zinc may increase resilience to traumatic brain injury, making it potentially useful in populations at risk for injury. It would appear that this is especially true for injuries to the temporal lobe.

A July publication of The Journal of Neurosurgery found that supplementing rats with EPA/DHA fish oil after head injuries reduced the observed issues with a concussion; “Animals receiving the daily fish oil supplement for 30 days post-concussion had a greater than 98 percent reduction in brain damage compared with the animals that did not receive the supplement. It is hypothesized that the omega-3 fatty acids in the fish oil reduced the neural inflammation induced by the concussion injury.”

Current studies suggest that oxidative stress lasts at least 24 hours after a traumatic brain injury and that antioxidant reserves like vitamin C are severely compromised. Vitamin C has been shown to prevent excitotoxic damage caused by excessive extracellular glutamate and increase GABA receptor function.

An animal study found that that vitamin D3 may play a role in mechanisms relevant to protective properties against the neurotoxicity of glutamate through upregulation of VDR expression.

Studies show that brain magnesium levels fall 50% for 5 days after injury to the CNS. Studies of both animal and human brain trauma victims suggest higher magnesium levels are associated with better recovery. Post-traumatic administration of magnesium to restore normal magnesium homeostasis reduces neuronal cell death and increases the likelihood of recovery.

Melatonin has been evaluated to be effective in TBI where it improves mood and behavior, decreases brain edema, decreases intracranial pressure and significantly increased superoxide dismutase and glutathione peroxidase (both reduce inflammation).

University of Buffalo researchers published a study in the Clinical Journal of Sports Medicine that individualized exercise programs just below the onset of symptoms is safe and can relieve nearly all post- concussion symptoms. The athletes who exercised returned to normal within 11 to 36 days, while those who did not exercise required 41 to 112 days of intervention.

Please review BDNF and APOE genotypes for a more detailed assessment of head injury recovery.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>MAO-A</b></p> <p>MAO-A (Monoamine oxidase A) is a critical enzyme involved in breaking down important neurotransmitters such as serotonin, estrogen, norepinephrine, and dopamine.</p>	MAO-A-rs6323			GG
<p><b>5-HT2A</b></p> <p>The 5-HT2A gene encodes for serotonin receptors found in the brain and central nervous system and is concentrated in the brain region essential for learning and cognition. Polymorphisms in rs6314 may result in reduced episodic memory in young and middle-aged individuals.</p>	5-HT2A-rs6314	GG		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>5-HT2A</b></p> <p>The 5-HT2A gene encodes for serotonin receptors found in the central nervous system. Polymorphisms in rs6311 and rs6313 may contribute to a reduced capacity to regulate stress, low vagal tone, anxiety, depression, OCD, and IBS, especially in females.</p>	5-HT2A-rs6311	CC		
	5-HT2A-rs6313	GG		
<p><b>COMT V158M</b></p> <p>COMT is connected to dopamine, adrenaline, estrogen and catecholamine metabolism.</p>	COMT V158M-rs4680		AG	
	COMT-rs4633		CT	
<p><b>ANKK1</b></p> <p>ANKK1 modulates the density of dopamine receptors in the brain.</p>	ANKK1-rs1800497		AG	
<p><b>DAO C2029G</b></p> <p>DAO participates in the degradation of extracellular histamine. This gene is connected to migraines.</p>	DAO C2029G-rs1049793		CG	
<p><b>HNMT C314T</b></p> <p>Histamine N-methyltransferase (HNMT) is a histamine-metabolising enzyme expressed in the brain. This gene is connected to migraines.</p>	HNMT C314T-rs11558538		CT	
<p><b>HNMT</b></p> <p>Histamine N-methyltransferase (HNMT) is a histamine-metabolising enzyme expressed in the brain. This gene is connected to hyperactivity and food dyes.</p>	HNMT-rs1050891		AG	
<p><b>FAAH</b></p> <p>FAAH (fatty acid amide hydrolase) is a gene that encodes for anandamide breakdown, a neurotransmitter and endogenous cannabinoid.</p>	FAAH-rs324420	CC		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>PEMT</b></p> <p>Choline is required for acetylcholine, a neurotransmitter of the vagus nerve that innervates numerous organs.</p>	PEMT-rs7946		CT	
	PEMT-rs12325817	CC		
<p><b>GAD1</b></p> <p>GAD1 stands for "Glutamate Decarboxylase 1" and is responsible for the conversion of glutamate to GABA.</p>	GAD1-rs3749034		AG	
<p><b>BDNF</b></p> <p>BDNF is a synaptic modulator of glutamate while GABA synapses are also regulated by BDNF.</p>	BDNF-rs6265	CC		
<p><b>SLC17A7</b></p> <p>SLC17A7 mediates the uptake of glutamate into synaptic vesicles at presynaptic nerve terminals of excitatory neural cells in the brain. Polymorphisms are associated with delayed recovery time from head injuries.</p>	SLC17A7-rs74174284			GG
<p><b>APOE</b></p> <p>Apolipoprotein E (APOE) is a lipid binding protein that transports triglycerides and cholesterol in multiple tissues, including the brain.</p>	APOE-rs429358	TT		
	APOE-rs7412			CC
<p><b>GAD1</b></p> <p>GAD1 stands for "Glutamate Decarboxylase 1" and is responsible for the conversion of glutamate to GABA.</p>	GAD1-rs3791851	TT		
	GAD1-rs2241165		CT	
	GAD1-rs3791850		AG	
	GAD1-rs769407	GG		

# DETOXIFICATION

## Liver Enzyme-CYP1A2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
CYP1A2 C164A rs762551	Homozygous AA

### Recap



Improves CYP1A2 Gene Function: Unfiltered fermented drinks (Kombucha, beer, wine), hops, marinades, cruciferous vegetables, blueberries, blackberries, red grapes, kiwi, watermelon, parsley, and spinach.



Decreases CYP1A2 Gene Function: Heterocyclic amines, nitrosamines, aflatoxin B1, polycyclic aromatic hydrocarbons, dioxins, and l-naphthoflavone. Omeprazole and primaquine are inducers. Caffeine and Tylenol combined with these compounds can make the effect worse.

## LIVER ENZYME-CYP1A2

**Research:** Approximately 200 polymorphisms exist in CYP1A2 gene region, with numerous studies focusing on rs762551. You have the homozygous (AA) rs762551 genotype, which is the rapid metabolizer.

The cytochromes P450 liver enzymes play an important role in the development of various cancers since they are involved in the metabolic transformation of numerous endogenous and exogenous compounds including carcinogens. CYP1A2 is a key factor in the metabolic activity of carcinogenic aromatic and heterocyclic amines, and researchers have found that the inhibition activity of this enzyme may represent a logical strategy for preventing the development of human cancers induced by the aromatic and heterocyclic amines. Further research has shown a cumulative value of phase I (CYP-450 enzymes) and phase II enzymes (GSTM1, GSTP1 and NAT2) in determining individual carcinogenic potential of compounds.

Heterocyclic amines (HCAs) are created by high heat reacting with the proteins. The way to reduce HCAs is to use marinades. Marinades reduce HCAs by up to 90 percent. For further protection, pair with cruciferous vegetables (especially fermented like sauerkraut) and an unfiltered beer or Kombucha due to the protection of the yeast. Red wine, blueberries, blackberries, red grapes, kiwi, watermelon, parsley, and spinach all inhibit the mutagenic activity of certain HCAs in vitro.

High antioxidant fruits, lemon juice, herbs, and spices help keep meat fresh and juicy while protecting against HCAs and reducing AGEs.

Grass-fed meat is higher in vitamin E, and in a study adding concentrations of vitamin E to the surface of ground beef reduced HCA production by 70%. Aim for medium to medium-rare for red meat, flip often and avoid burning. The darker the color the higher the HCA concentrations.

Nitrosamines are used in pesticides, created by frying meat, and from a conversion in the gut by nitrites from cured meats. Vitamin C prevents nitrites from becoming nitrosamines. Limit cured meat consumption using nitrites and take vitamin C when needed.

Aflatoxin B1 is the most common in food and amongst the most potent genotoxic and carcinogenic. It can occur in grain-fed milk, nuts/grains stored in hot conditions or bins, vegetable oils, cocoa or coffee beans stored in warm conditions, and dried fruit. We don't recommend Brazil nuts because they are prone to aflatoxin contamination. Choose nuts and seeds in sealed bags, preferably sprouted. You also want to minimize or avoid oats (unless tested free of ochratoxin). Low protein diets may increase the toxicity of aflatoxin and promote cancerous growth.

Hops in beer contain a flavonoid called xanthohumol, which strongly inhibits CYP1A2. Xanthohumol has anti-carcinogenic properties and has been found to scavenge reactive oxygen species, including hydroxyl- and peroxy radicals, and to inhibit superoxide anion radical and harmful nitric oxide production.



## 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.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>CYP1A1*2C 4889</b></p> <p>CYP1A1 is in the estrogen metabolism pathway along with CYP1B1, CYP1A2, CYP31A, SULT's and COMT. CYP1A1 is involved in the metabolism of benzopyrene.</p>	CYP1A1*2C 4889-rs1048943	TT		
<p><b>CYP1A2 C164A</b></p> <p>CYP1A2 metabolizes various environmental procarcinogens, such as heterocyclic amines, nitrosamines, aflatoxin B1 and ochratoxin A.</p>	CYP1A2 C164A-rs762551			AA
<p><b>CYP1B1*6 L432V</b></p> <p>The CYP1B1 gene metabolizes pro-carcinogens such as polycyclic aromatic hydrocarbons and 17 beta-estradiol.</p>	CYP1B1*6 L432V-rs1056836	GG		
<p><b>CYP2C9*3 A1075C</b></p> <p>Variants in CYP2C9 rs1057910 may alter the metabolism of THC, the psychoactive compound found in cannabis.</p>	CYP2C9*3 A1075C-rs1057910	AA		
<p><b>CYP2D6 T100C</b></p> <p>CYP2D6 metabolizes approximately 50% of drugs in clinical use.</p>	CYP2D6 T100C-rs1065852	GG		
<p><b>CYP2E1</b></p> <p>Research has identified CYP2E1 as the primary P450 isozyme responsible for benzene metabolism at low concentrations, acrylamide to glycidamide, alcohol, Tylenol, and nitrosamines.</p>	CYP2E1-rs2031920	CC		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>CYP3A4*1B</b></p> <p>The CYP3A4 enzyme is involved in the metabolism of approximately 50% of drugs that are used today, cholesterol homeostasis, and the oxidative deactivation of testosterone.</p>	CYP3A4*1B-rs2740574	TT		
<p><b>CYP2C19*17</b></p> <p>Genetic variability impacts expression and activity of CYP2C19 and therefore can influence drug metabolism and catabolism of estrogens.</p>	CYP2C19*17-rs12248560			TT
<p><b>NAT2</b></p> <p>The NAT2 gene encodes an enzyme that functions to activate and deactivate arylamine, hydrazine drugs, and carcinogens.</p>	NAT2-rs1495741		AG	
<p><b>VKORC1*2</b></p> <p>Variants in VOKRC1*2 may increase the need for vitamin K2 and a sensitivity to dosing of the drug Warfarin.</p>	VKORC1*2-rs9923231	CC		
<p><b>COQ2</b></p> <p>The COQ2 gene encodes an enzyme that functions in the final steps in the biosynthesis of CoQ10 and homozygous variants may increase the risk of statin induced myopathy.</p>	COQ2-rs4693596		CT	


# CARDIOVASCULAR HEALTH AND ATHLETIC PERFORMANCE


## Power and Recovery-ACTN3

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ACTN3 rs1815739	Homozygous TT

## Recap

 Improves ACTN3 Gene Function: Not applicable for ACTN3.

 Decreases ACTN3 Gene Function: Not applicable for ACTN3.

## POWER AND RECOVERY-ACTN3

The XX (TT) genotype is a loss-of-function variant that results in a complete lack of expression of  $\alpha$ -actinin-3 and Type II muscle fibers; the deficiency occurs in approximately 20% of the world's population. The X allele can be traced back over a million years. The frequency correlates with higher latitude and lower temperature, showing a possible selection for cold tolerance and famine. Researchers found that the selection of XX appears to be for more fatigue-resistant muscles that generate heat from activation of brown adipose tissue, providing a tentative explanation for the evolutionary advantage of carrying the XX genotype in a cold climate.

The XX genotype frequency differs across ethnic groups. Approximately 25% of Asians, 18% of Caucasians, 11% of Ethiopians, 3% of Jamaican and US African Americans, and 1% of Kenyans and Nigerians possessing the XX genotype.

Studies in both Ironman athletes and ultra runners found that the XX genotype experienced the most amount of muscle pain and damage after the competition as measured by serum concentrations of myoglobin, creatine kinase, lactate dehydrogenase, and aspartate aminotransferase. However, there was no difference in race time or perceived exertion between all three genotypes.

ACTN3 XX homozygotes presented higher serum creatine kinase concentrations and self-reported pain scores than RR homozygotes after 20 maximal eccentric knee extensions. The same was true of soccer players after an eccentric training practice that included jumps, changes of direction, accelerations, and decelerations. However, it was not true with eccentric elbow flexion exercise or drop jumps, showing that specific lower body activities may be the most relevant. Your IL6 gene should be assessed, which could compound or reduce creatine kinase levels.

Numerous studies have shown that the XX genotype has a higher risk of ankle injuries and that XX genotypes were 2.6 times more likely to suffer an injury than RR genotypes. These injuries were also more likely to be of increased severity.

Of the eight studies identified that examined the impact of this polymorphism on post-exercise muscle damage, six reported that that the XX genotype was associated with higher levels of markers associated with muscle damage.

Both alpha-actinin-3 (encoded for by ACTN3) and alpha-actinin-2 are major structural components of the Z-disks within muscle fibers. The Z-disk itself is vulnerable to injury during eccentric contractions, and ACTN3 deficiency may increase this vulnerability with eccentric contractions in the ankle and hamstring.

More attention is recommended to strengthen the ankles and hamstrings (Nordic hamstring exercise) and post-workout recovery methods for injury prevention in the XX genotype. While the Nordic hamstring exercise is recommended due to the eccentric movement, the XX genotype would have increased muscle soreness and damage following this exercise, making timing and recovery days key within a training program.

Researchers have stated that the ACTN3 genotype could be utilized alongside other well-established markers to determine training intensity in the days following a match. Players genetically predisposed to increased muscle damage, either having a

more extended recovery period or increased recovery interventions such as cold-water immersion.

Exercise phenotypes have played a key role in ensuring survival over human evolution. The saying "life is a marathon, not a sprint," could describe ACTN3 and endurance genes. Elite endurance athletes tend to live longer than power athletes, and genotypes related to endurance performance may also be correlated with living over 100.


The ACTN3 genotype of centenarians resembles that of world-class elite endurance athletes and differs from that of elite power athletes. Researchers suggest a specific 'survival' advantage brought about by alpha-actinin-3 deficiency and the endurance oxidative muscle phenotype with other benefits still being explored.


## VO2 Max-PPARGC1A

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
PPARGC1A rs8192678	Heterozygous CT

### 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 CT

### 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	Homozygous AA

## 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 homozygous AA genotype and are a "rapid metabolizer" of caffeine. This means that caffeine will quickly be metabolized from your body and the effects lasting a shorter period of time. It is important to review your COMT gene function to better understand a sensitivity to coffee intake.


For the AA genotype, caffeine decreased 40-km time in cyclists by an average of 3.8 minutes in the AA homozygotes as compared to 1.3 minutes in the C allele carriers.

## Potassium and Magnesium-ADD1


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ADD1 rs4961	Heterozygous GT

## 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.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>ACTN3</b></p> <p>ACTN3 encodes for the alpha-actin-3 protein found exclusively within type-II fast-twitch muscle fibers.</p>	ACTN3-rs1815739			TT
<p><b>PPARGC1A</b></p> <p>It has been demonstrated that variants in the PPARGC1A gene affect the exercise-induced change in maximal oxygen uptake (VO2).</p>	PPARGC1A-rs8192678		CT	
<p><b>IL6</b></p> <p>IL6 is an interleukin that acts as both a pro-inflammatory cytokine and an anti-inflammatory myokine.</p>	IL6-rs1800795			GG



Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>SOD2</b></p> <p>Superoxide dismutase (SOD2) is manganese dependent and protects against superoxide for the mitochondria of the cell. The homozygous genotype increases the need for antioxidant support in high-intensity athletes.</p>	SOD2-rs4880		AG	
<p><b>COL1A1</b></p> <p>COL1A1 produces alpha 1 chain of type I collagen, a major protein in tendons and ligaments.</p>	COL1A1-rs1800012	CC		
<p><b>PON1</b></p> <p>PON1 (Paraoxonase) plays a large role in removing pesticides. It is also involved with supporting HDL function and LDL oxidation.</p>	PON1-rs662		CT	
<p><b>LPA</b></p> <p>Lp(a) is a sticky form of LDL that appears to affect plaque growth, LDL particle size and increase the risk of plaque rupture and blood clotting.</p>	LPA-rs3798220	TT		
<p><b>CYP1A2 C164A</b></p> <p>Variants in CYP1A2 determine caffeine metabolism and effects on bone density and cardiovascular health.</p>	CYP1A2 C164A-rs762551			AA
<p><b>9p21</b></p> <p>9p21 is considered an important genetic marker for cardiovascular health.</p>	9p21-rs4977574		AG	
<p><b>FADS1</b></p> <p>FADS1 is involved in fatty acid metabolism, and variants in this gene are associated with elevated triglyceride levels.</p>	FADS1-rs174546	CC		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>F5</b></p> <p>Variants in F5 increase the risk of deep vein thrombosis, especially if using oral contraceptives.</p>	F5-rs6025	CC		
<p><b>ADRB2</b></p> <p>Beta-2 adrenergic receptor (ADRB2) is abundantly expressed in cardiac cells, and bronchial smooth muscle cells and is connected to stress levels and heart health.</p>	ADRB2-rs1042713	GG		
<p><b>ACE1 G2350A</b></p> <p>ACE1 is part of the renin-angiotensin system responsible for the conversion of angiotensin I to angiotensin II, constricting blood vessels and elevating blood pressure.</p>	ACE1 G2350A-rs4343		AG	
<p><b>ADD1</b></p> <p>Variants in ADD1 are associated with hypertension in Asians.</p>	ADD1-rs4961		GT	
<p><b>AGTR1</b></p> <p>Angiotensin-II receptor type 1 (AGTR1) is a major component of the renin-angiotensin system for regulating blood pressure and is highly expressed in adipose tissue, liver, leukocytes and the intestine. The homozygous genotype may increase the risk of high blood pressure from excess dietary fat and carbohydrate intake.</p>	AGTR1-rs5186	AA		
<p><b>ACE2 A8790G</b></p> <p>ACE2 is part of the renin-angiotensin system, responsible for degrading angiotensin II and providing balance to ACE1 by dilating blood vessels and lowering blood pressure.</p>	ACE2 A8790G-rs2106809	AA		

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>TMPRSS2</b></p> <p>Transmembrane Serine Protease 2 is highly expressed in the prostate and lungs, and the expression is associated with viral susceptibility and prostate cancer.</p>	<p>TMPRSS2-rs2070788</p>			<p>AA</p>

# DNA PROTECTION, DAMAGE & REPAIR

## DNA Repair-ATM

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
ATM D1853N rs1801516	Homozygous AA

## Recap



Improves ATM Gene Function: Folate, higher nut, vegetable and fruit intake, exercise, and intermittent fasting (waiting 13-16 hours to eat from dinner to breakfast).



Decreases ATM Gene Function: Smoking, obesity (especially abdominal fat), diabetes, binge drinking, chronic pancreatitis, heterocyclic amines, polycyclic aromatic hydrocarbons and isolated fructose.

## DNA REPAIR-ATM

**Research:** People who have a variants in the ATM gene will benefit from nutrients that have been found in studies to improve DNA repair in regards to pancreatic health. While early studies linked ATM gene variants to breast health, further research has shown conflicting results, with ATM variants being potentially only being relevant when coupled with other genes like BRCA-1 and BRCA-2 and familial breast cancer.

DNA repair is needed when cells are harmed by sunburns, chemicals, toxins and stress. Efficient repair of damaged DNA strands helps maintain the stability of the cell's genetic DNA. DNA repair enzymes are typically working poorly in families with a lot of cancer and require more support. Nutrition plays a major role in DNA repair enzymes.

### Pancreatic Health

The risk for pancreatic cancer goes up with diabetes. One study found that compared to non-diabetics with the ATM D1853N normal GG genotype, diabetics carrying the ATM D1853N GA/AA genotypes had more than triple the risk of developing pancreatic cancer. This makes stabilizing blood sugar a priority.

Studies have found that a high dietary intake of fresh fruit and vegetables reduced the risk of developing pancreatic cancer, and recent epidemiological studies have associated nut consumption with a protective effect against it.

One cohort study found a significantly decreased risk of pancreatic cancer by 55% for the highest levels of dietary folate compared with the lowest. Another cohort found that the highest blood folate levels showed a significantly decreased risk compared to the lowest. Folic acid supplements did not show a protective effect in these studies.

Review your genes for blood sugar, insulin, and folate.

### Breast and Ovarian Health

If breast cancer runs in your family and you have done BRCA testing, the following research will be helpful in your nutrition plan. BRCA-1 and BRCA-2 are tumor suppressor genes that are responsible for DNA repair and linked to breast and ovarian health. It is the reduced function with certain variants that causes impaired DNA repair. BRCA1-associated tumors commonly display a triple-negative (TN) phenotype lacking expression of estrogen receptor (ER), progesterone receptor (PR) and the human epidermal growth factor receptor 2 (HER2).

Research has found that women with the BRCA-1 and BRCA-2 mutations who consumed up to 27 different fruits and vegetables a week (variety important) saw their cancer risk diminish by fully 73 percent. Selenium and choline have both been found to improve BRCA-1 and BRCA-2 function and lower the risk of breast cancer. Iodine also plays a special role in breast health. Check your PEMT gene function to see your need for choline.

The compound luteolin found in celery, broccoli, thyme and parsley was found in animal studies to kill cancer cells, stop triple-negative cells spreading to the lungs and block spreading throughout the body. Another study found that blueberry extract decreased proliferation of triple-negative breast cancer cell lines.

Lignans are highest in flax seeds and research shows that women who have the highest level of lignans in their body have the lowest risk of breast cancer. In postmenopausal women, lignans can cause the body to produce less active forms of estrogen.

Animal studies have shown that both flaxseed oil and lignans can reduce breast tumor growth and spread, even for ER negative cancer cells. One study in mice concluded that flaxseed inhibited the growth of human estrogen-dependent breast cancer.


Another study found that enoki mushroom extract was shown to inhibit the growth of both estrogen-receptor positive (ER+) MCF-7 and estrogen-receptor negative human breast cancer cell lines. Furthermore, the extract inhibited breast cancer cell colony formation by 99%.

### Processed Meat and Colon Cancer-GATA3


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
GATA3 rs4143094	Heterozygous GT

### Recap



Improves GATA3 Gene Function: Avoiding processed meats.



Decreases GATA3 Gene Function: Processed meats like hot dogs, cured meats, pepperoni and sausages.

### PROCESSED MEAT AND COLON CANCER-GATA3

**Research:** A large-scale genome-wide analysis of over 18,000 people from the U.S., Canada, Australia and Europe found that variants in GATA3 (rs4143094) was associated with an increased risk of colon cancer for those eating processed meat compared to those with the normal genotype.

A meta-analysis revealed that by raising the serum level of vitamin D to 34 ng/ml, the incidence rates of colorectal cancer could be reduced by half. Researchers projected a two-thirds reduction in incidence with serum levels of 46 ng/ml, which corresponds to a daily intake of 2,000 IU of vitamin D3.

All of the foods below have been found in research studies to reduce the risk of colon cancer: black raspberries, blackberries, raspberries, cranberries, blueberries, apples, oranges, avocado, tomatoes, garlic, onions, shallots, leeks, cabbage, sauerkraut, broccoli, Brussels sprouts, sweet potatoes, beets, spinach, kale, asparagus, cauliflower, turmeric, rosemary, oregano, basil, thyme and parsley. Preventing constipation should be a priority.

### Longevity-SIRT1

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
SIRT1 rs7895833	Wild Type AA

## Recap



Improves SIRT1 Gene Function: Exercise, fasting, 7-8 hours of sleep per night, sauna, polyphenols, vitamin D, omega-3 fatty acids, resveratrol, magnesium, and melatonin.



Decreases SIRT1 Gene Function: The APOE-e4 genotype, high blood sugar, and insulin resistance.

## LONGEVITY-SIRT1

**Research:** SIRT1 regulates numerous genes that accelerate the aging process, modulate DNA repair mechanisms and transcription factors like p53 (tumor suppressor gene), FOXOs (key regulators of lipid metabolism, stress resistance, and apoptosis) and inhibits NF- $\kappa$ B, a pathway connected to viral inflammation.

SIRT1 activity goes down as we age, and DNA damage accumulates, and its activity is especially harmed by a sedentary lifestyle, poor diet, and obesity. Activation of sirtuins induces the growth of blood vessels, insulin sensitivity and better glucose control, and other health benefits in a wide range of age-related cardiovascular and metabolic disease models. Experimental models have shown that increasing the activity of the sirtuins is associated with the delay of age-related diseases and potentially increasing longevity.

Researchers have observed a significant increase in SIRT1 levels in longevity populations and found a significant positive correlation between SIRT1 levels and age in a Turkish population. The oldest people carrying AG genotypes for rs7895833 had the highest SIRT1 level compared to the AA genotype, suggesting an association between rs7895833 SNP and lifespan longevity.

The average age of older people carrying AG genotype ( $76.0 \pm 1.5$  years) was significantly higher than the average age of older people carrying AA genotype ( $71.3 \pm 1.4$  years).

Your APOE genotype may also affect SIRT1 activity for longevity. Research from the Buck Institute group found that APOE-e4 reduced expression of SIRT1. The reduced expression of SIRT1 was thought to impair beta-amyloid clearance observed in Alzheimer's. If you have the APOE-e4 allele, the AA SIRT1 genotype may require more SIRT1 activation.

Polyphenols are activators of SIRT1 and contain anti-inflammatory and apoptosis properties. These include piceatannol (a metabolite of resveratrol), olive oil, fisetin (strawberries, apples, grapes), quercetin (wine, peppers, berries, apples) and resveratrol (wine, blackberries, blueberries, pistachios and dark chocolate).

Other activators of SIRT1 that also benefit the APOE-e4 carriers include magnesium, melatonin, vitamin D, and omega-3 fatty acids. One study found that centenarians (those living over 100) have higher total body magnesium and lower calcium levels than most elderly people.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<b>XRCC3</b> XRCC3 participates in DNA double-strand break/recombination repair.	XRCC3-rs861539		AG	
<b>ATM D1853N</b> ATM coordinates DNA repair by activating enzymes that fix double stranded DNA breaks.	ATM D1853N-rs1801516			AA

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>ESR2</b></p> <p>ESR2 acts as a tumor suppressor gene that codes for estrogen receptor beta (ER-beta), one of two main types of estrogen receptor activated by estrogen. ESR2 is strongly expressed in the prostate.</p>	ESR2-rs2987983	AA		
<p><b>TP53</b></p> <p>TP53 is a tumor suppressor gene responsible for DNA repair.</p>	TP53-rs1042522		CG	
<p><b>MDM2</b></p> <p>Variants in the MDM2 gene encode a protein that reduces cellular levels of the p53 tumor suppressor protein.</p>	MDM2-rs2279744	TT		
<p><b>MLH1</b></p> <p>MLH1 codes for a DNA repair enzyme linked to colon health.</p>	MLH1-rs1800734	GG		
<p><b>GATA3</b></p> <p>GATA3 factors are involved in cellular maturation with proliferation arrest and cell survival.</p>	GATA3-rs4143094		GT	
<p><b>SIRT1</b></p> <p>SIRT1 senses changes in intracellular NAD+ levels and plays a role in DNA damage and repair.</p>	SIRT1-rs7895833	AA		


# METHYLATION CYCLE


## Folate-MTHFR 677

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
MTHFR 677 rs1801133	Heterozygous AG

## Recap

 Improves MTHFR 677 Gene Function: Riboflavin and methylfolate.

 Decreases MTHFR 677 Gene Function: Proton pump inhibitors, oral contraceptives, NSAIDs, anticonvulsants, antivirals, antibiotics, acid blockers/antacids and hypothyroidism.

## FOLATE-MTHFR 677

The frequency of the 677 polymorphism of MTHFR in the Caucasian population is up to 50% heterozygous.

The heterozygous MTHFR 677 has a 30% reduced function, potentially creating a higher need for dietary methylfolate depending on climate, skin tone and sun exposure, and dietary B2, choline, betaine, B6 and B12 intake. Variants in MTHFR 677, especially the homozygous genotype, are higher in Mediterranean climates and malaria-endemic regions like Southeast Asia. Researchers believe these variants were selected to protect against UV-induced DNA damage and malaria.

While a heterozygous MTHFR 677 and MTHFR 1298 have been associated with higher homocysteine levels, not all people will develop high homocysteine levels.

Homocysteine is a non-protein amino acid that is created and recycled in the methylation cycle. Sluggish enzymes in the cycle can cause elevated levels in the blood, which can cause inflammation in the blood vessels. High homocysteine has been implicated in amyloid buildup, DNA damage and cancer, mitochondrial dysfunction, cardiovascular disease, age related macular degeneration, apoptosis of neurons and depression. BH4 structurally resembles folate and has been described to be reduced in endothelial cells when increased levels of homocysteine are present. Stabilizing MTHFR with B2 and targeting

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.

A large meta-analysis showed the lack of statistically significant association between MTHFR mutations and coronary heart disease except in the Middle East and Japan, where it portrayed statistical significance.

It is important to consider riboflavin intake, PEMT, MTR/MTRR, and CBS activity to assess overall homocysteine metabolism. Too high or too low levels of B12, B6, folate or their co-factors may cause dysregulation of methyl donor activity.


## Folate-MTHFD1 G1958A

Below is a summary of your most significant variant genotypes:




GENE	GENOTYPE
MTHFD1 G1958A rs2236225	Heterozygous AG

## Recap



Improves MTHFD1 Gene Function: 5-formyl-tetrahydrofolate (folinic acid) and choline



Decreases MTHFD1 Gene Function: Folate and choline deficiency, proton pump inhibitors, oral contraceptives, NSAIDs, anticonvulsants, antivirals, antibiotics, and acid blockers/antacids.

## FOLATE-MTHFD1 G1958A

**Research:** A meta-analysis strongly suggests that the MTHFD1 G1958A polymorphism might be associated with maternal risk for neural tube defects in Caucasian populations. However, the evidence of this association should be interpreted with caution due to the selective nature of publication of genetic association studies. Another study found that the polymorphism decreases enzyme stability and increases risk of congenital heart defects.

5-formyl-tetrahydrofolate is the second most common type of folate after methylfolate in the certain foods. This is why dietary folate is optimal because it addresses both upstream and downstream folate gene polymorphisms in the methylation cycle.


Checking MTHFR and PEMT genes along with MTHFD1 helps you determine your requirements for folinic acid, methylfolate and choline to help stabilize enzymatic function.

## B12-MTRR


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
MTRR A66G rs1801394	Homozygous GG

## Recap



Improves MTRR Gene Function: B12, B6 and folate.



Decreases Gene Function: Antacids, antibiotics, proton pump inhibitors, Metformin, anticonvulsants, oral contraceptives, certain psychiatric medications, yeast overgrowth and poor FUT2 function.

## B12-MTRR

**Research:** Methionine synthase reductase (MTRR) is a vital enzyme of homocysteine/methionine metabolic pathway and is required for the conversion of inactive form of methionine synthase (MTR) to its active form. MTRR helps recycle B12. If MTR is working 100%, MTRR variants may be less pronounced. Variants in both MTR and MTRR may lead to issues with B12.

A clinically important allelic variant of MTRR A66G, with less enzymatic activity is reported with worldwide prevalence rate of 30%. The very high frequency of the homozygous genotype (greater than normal allele) was reported from Italy, France, Ireland, Netherlands and India.

Several epidemiological and case control studies have reported that the GG genotype may be a risk factor for several disease/disorders like neural tube defects, Down syndrome, coronary artery disease, male infertility and cancer through sustained hypomethylation if not addressed. An additional effect is a decreased availability of folate. Several studies show that DNA hypomethylation is the main causative factor of defective gene expression.

Caucasians with late life depression who were homozygous (GG) were more likely to still be depressed after a course of SSRI

antidepressant treatment compared to individuals who are homozygous at the A allele or who were AG heterozygotes. This points toward the hypothesis that factors which elevate homocysteine concentrations have an adverse effect on depression treatment response.


Heterozygous or homozygous variants in MTRR may require more B6, folate and B12 if combined with MTHFR 677 and MTR variants. If you suffer from migraines, B6, folate and B12 may be effective in reducing migraines. Research has also found B6, folate and B12 to help prevent macular degeneration.


## B12-TCN2

Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
TCN2 C766G rs1801198	Homozygous GG

## Recap

 Improves TCN2 Gene Function: Lithium.

 Decreases TCN2 Gene Function: Depleted lithium levels.

## B12-TCN2

**Research:** Low vitamin B12 concentrations in the cell can be the result of low vitamin B12 intake, but they can also be attributable to a disturbance in the absorption, transport, or cellular uptake of this vitamin. High B12 levels on blood tests may indicate poor intracellular transport and absorption.

Approximately 20-25% of circulating cobalamin binds to transcobalamin 2 (TCN2), which is referred to as active vitamin B-12. A 2017 meta-analysis found that subjects with the rs1801198 GG genotype had significantly lower concentrations of holotranscobalamin and higher concentrations of homocysteine (European descent only) than subjects with the CC genotype.

In Chinese patients, the CG and GG genotypes were higher in patients with mild, moderate, and severe ulcerative colitis compared with those with remission ulcerative colitis. The average homocysteine level was elevated, whereas the average vitamin B12 and folate levels were reduced.

If you have the GG TCN2 genotype, you may require more dietary lithium to assist B12 transport. Lithium ranges widely based on the water supply. It is highest in certain mineral waters, shellfish, tomatoes, spinach, unpeeled potatoes, eggplant, cabbage, rooibos tea, rosehips, pastured eggs and *Saccharomyces cerevisiae* (yeast). Countries that consume the most lithium include the inhabitants of China, Mexico, Austria, and Sweden.

Testing lithium levels may be a useful marker for certain disorders like depression and bipolar disorder. One study found that young US children with autism and their mothers had unusually low levels of lithium compared to neurotypical children and their mothers.

Researchers have also explored lithium's role in preventing cancer metastasis when cancer cells are expressing high levels of TGFβ1p. Inhibition of TGFβ1p expression in cancer cells by lithium decreased tumor metastasis to the lungs, liver, and lymph nodes.


Be aware that high B12 supplementation depletes lithium levels, and dosing lithium supplementation should be done with extreme caution due to its suppressing effect on the thyroid hormones.

## Choline-PEMT


Below is a summary of your most significant variant genotypes:

GENE	GENOTYPE
PEMT rs7946	Heterozygous CT
PEMT rs12325817	Wild Type CC

## Recap



Improves PEMT Gene Function: Choline, vitamin C and estrogen.



Decreases PEMT Gene Function: Nighttime pain relievers, antihistamines, anti-seizure medications, sleep aids, antidepressants, incontinence drugs and narcotic pain relievers.

## CHOLINE-PEMT

**Improves PEMT Gene Function:** Choline, vitamin C and estrogen.

**Decreases Gene Function:** Nighttime pain relievers, antihistamines, anti-seizure medications, sleep aids, antidepressants, incontinence drugs and narcotic pain relievers.

**Research:** Phosphatidylethanolamine-N methyltransferase (PEMT) catalyzes the synthesis of phosphatidylcholine.

Choline is responsible for shuttling fat out of the liver, aiding the gallbladder, healthy cell membranes to protect against inflammation, lowering anxiety, preventing damage from glutamate spikes, deep sleep, healthy DNA, healthy pregnancy and breast health. Non-Alcoholic Fatty Liver Syndrome occurs mainly from a choline deficiency. Choline deficiency also increases sensitivity to carcinogenic chemicals, mycotoxins and vegetable oils due to poor cell membrane health.

Research shows that the highest dietary intake of choline is found from people in the Northern countries, whereas Mediterranean countries had the lowest intake. Worldwide, total choline intake in adults ranges from 284 mg/day to 468 mg/day for men, from Taiwan and Sweden, respectively; and from 263 mg/day to 374 mg/day for women, from Mexico and Sweden. Major food sources of dietary choline vary by country. For example, eggs, meat, and dairy are the major sources of total dietary choline in New Zealand, while eggs, seafood, meats, and soy products are the predominant sources in Japan and China.

Having one or more T alleles at rs7946 is associated with having lower phosphatidylcholine production in the liver.

More than 40% of women have a genetic polymorphism in PEMT (rs12325817) that makes this gene unresponsive to estrogen, which creates the same high choline requirement as men. These women may be especially sensitive to dietary choline variations during pregnancy. One study found that the highest quintile of choline consumption was associated with a lower risk of breast cancer compared with the lowest quintile.

Eighty percent of the women who were homozygous for the rs12325817 SNP manifested signs of choline depletion (liver or muscle dysfunction), relative to 43% of subjects carrying one copy of the variant allele and 13% of subjects without the SNP. Almost 75% of the North Carolina population in the United States has one variant allele.

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>MTHFR 677</b></p> <p>The MTHFR 677 gene encodes the MTHFR gene to convert folate into the active form, methylfolate. Variants in this gene slow down enzymatic function.</p>	MTHFR 677-rs1801133		AG	

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>MTHFR 1298</b></p> <p>MTHFR 1298 is involved in converting 5-methylfolate (5MTHF) to tetrahydrofolate (THF). Unlike MTHFR 677, the 1298 variant does not lead to elevated homocysteine levels unless paired with a heterozygous MTHFR 677.</p>	MTHFR 1298-rs1801131	TT		
<p><b>MTHFD1 G1958A</b></p> <p>(Methylenetetrahydrofolate dehydrogenase 1) encodes a protein that possesses three distinct enzymatic activities in the interconversion of 1-carbon derivatives of tetrahydrofolate.</p>	MTHFD1 G1958A-rs2236225		AG	
<p><b>DHFR A20965G</b></p> <p>Dihydrofolate reductase (DHFR) catalyzes the reduction of dihydrofolate to tetrahydrofolate (THF) and affect synthetic folic acid metabolism.</p>	DHFR A20965G-rs1643659	TT		
	DHFR C19483A-rs1677693	GG		
<p><b>MTR A2756G</b></p> <p>MTR (methionine synthase) combines folate, methyl B12 and homocysteine into methionine.</p>	MTR A2756G-rs1805087	AA		
<p><b>MTRR A66G</b></p> <p>MTRR attaches a methyl group to B12 and variants here will slow the process. When both MTR and MTRR exist, dysfunction can occur.</p>	MTRR A66G-rs1801394			GG
<p><b>TCN2 C766G</b></p> <p>Transcobalamin II (TCN2, or holotranscobalamin when bound) transports B12 to peripheral tissues. Variants in this gene may affect B12 transport.</p>	TCN2 C766G-rs1801198			GG

Gene & Gene Function	Gene Rsid	Wild Type	Heterozygous	Homozygous
<p><b>PEMT</b></p> <p>Variants in PEMT may increase the need for choline and increase the sensitivity to anticholinergic drugs.</p>	PEMT-rs7946		CT	
	PEMT-rs12325817	CC		
<p><b>CBS A13637G</b></p> <p>The Cystathione Beta-Synthase (CBS) enzyme pulls homocysteine to hydrogen sulfide (H2S) and glutathione, requiring B6 and SAMe as a modulator.</p>	CBS A13637G-rs2851391	CC		
<p><b>CBS</b></p> <p>The Cystathione Beta-Synthase (CBS) enzyme pulls homocysteine to hydrogen sulfide (H2S) and glutathione, requiring B6 and SAMe as a modulator. CBS rs234709 and rs4920037 assists in arsenic detoxification.</p>	CBS-rs234709		CT	
	CBS 191150T-rs4920037	GG		