Tenisha Hancock Functional Genomic Interpretation

Primary Health Concerns: Recurrent Miscarriage

Labs: Consistent slight elevations in MCV & MCH - blood levels of B12 and folate look decent, but I recommend doing urinary measurement (via OAT) to see how much is actually getting into the cells (as opposed to stuck in the blood, making levels look decent). Try supplementation with folinic acid (not folic) instead of methylfolate. Slightly elevated homocysteine may be helped by this as well. Elevated monocytes (viral) and low WBC and lower neutrophils and higher lymphocytes can indicate a chronic low-grade infection (bacterial or viral).

Overall Takeaways: Support mitochondrial health and antioxidant status (with a high recommendation for liposomal or S-Acetyl glutathione). I recommend urinary mycotoxin testing and OAT to gain clarity on blood markers and genetic predispositions. Also, phosphatidylcholine will help support bile flow, detoxification, and methylation, and is crucial during the first trimester of fetal development of the brain and nervous system.

The genes that I am mentioning in your personalized report are ones you have variations in that I consider to be more impactful or clinically relevant to you: Sort of like a 'highlight reel' of what I see to be your most impactful genetic variants. These may be ones relating to any symptoms or diagnoses you have or had, or they may be genetic SNPs you have that are more variated than the mean population of about 55,000 people in the software to compare you to. Each section has supplement, lifestyle, and/or dietary recommendations that have been shown to support the genes in that section. Since not all recommendations are going to resonate with you, and would be a LOT to do/take/get, you may opt to schedule a 1:1 consultation with me to help you decide which of the recommendations to start with, or which would be the "most bang for your buck."

If you have any questions or need help understanding this report, feel free to reach out and schedule a 1:1 consultation with me to discuss your results further!

Also, I have a chapter in my book that includes a myriad of things that can be done to improve health regardless of what your genetic profile looks like. If you're new to healthy living and would like further recommendations beyond what is offered here, I would suggest checking it out!

Fenton Reaction

Iron/Copper

Background Information-

Fenton Reaction and Iron Dysregulation

Your Genes:

SLC genes - SLC (Solute carrier) genes are responsible for transporting a range of substances, including ions, amino acids, carbohydrates, vitamins, and drugs, across the cell membrane. These membrane proteins are critical for numerous physiological processes such as nutrient uptake, waste removal, and maintaining cellular homeostasis. They are also important targets for drug development and have been linked to various diseases such as diabetes, cancer, and neurological disorders. Additionally, SLC genes are present in various tissues and organs throughout the body and play a critical role in regulating systemic metabolism.

SLC31A1 - SLC31A1 and SLC31A2 transport copper into the cells where it is utilized for various functions including enzymatic reactions and the synthesis of important proteins. Variants can cause copper to get stuck outside and create inflammation through the Fenton reaction (Hydroxyl radicals). This may also look like normal or elevated levels in the blood when there is actually suboptimal levels in tissue. However, it is important to note that copper balance in the body is tightly regulated and can be affected by many factors beyond SLC31A1 and SLC31A2 variants.
CP - Ceruloplasmin is what binds copper. Having a variated CP gene can cause lack of copper binding/utilization, and therefore poor iron regulation. Since ceruloplasmin, your copper binding protein, depends on retinol (the form of vitamin A that the body uses), I recommend cod liver oil or other non-beta carotene forms of vitamin A.

SLC11A2 - SLC11A2 is the divalent metal transporter that is involved in the absorption of iron and other divalent metals in the intestines. It moves positively charged iron atoms and other minerals as well (cobalt, manganese, copper and zinc). Variations in the SLC11A2 gene can lead to various conditions related to impaired iron absorption or transport. SNP's can result in poor gut absorption of iron. It can keep iron from getting in, get stuck and cause organ damage. SLC48A1 and SLC11A2 variants may not allow absorption. This may be protective if coupled with SLC40A1 variants.
SLC40A1 - SLC40A1 variants can cause iron to get stuck inside the cell. It is not uncommon to see low iron in blood work with SLC40A1 variants, because it's not taking iron out of the cell and into the blood. The liver is especially vulnerable to the accumulation of iron. SLC40A1 is not common to have variants. So even just a heterozygous variant is pretty significant., especially with Nrf2, glutathione, or KEAP1 variants.
G6PD - Glucose-6-phosphate dehydrogenase - G6PD enzyme is crucial for red blood cell function, protection against oxidative stress, and helps protect red blood cells from damage and premature destruction. SNPs can cause insufficiencies of the G6PD enzyme. G6PD is part of NADPH production and recycling (along with ME1, PGD, IDH1). NADPH is important for phase 1 liver detox (CYPs), for iron regulation, and for breakdown of heme, to name only a few functions. *If we have G6PD issues, we won't have enough NADPH and so won't recycle glutathione back to the necessary reduced form. Lack of G6PD and therefore NADPH makes red blood cells (RBC) more susceptible to reactive oxygen species free radicals, which may cause anemia and miscarriage and fetal problems.* The main function of G6PD is to provide reducing power (NADPH) and pentose phosphates for fatty acid nucleic acid synthesis. SNPs in G6PD will significantly impact NADPH level, independent of Nrf2 polymorphisms (which would throw fuel onto the fire). G6PD genes are involved in the processing of carbs and play a role in red blood cells, protecting them from damage.
G6PD is responsible for the first step in a chemical pathway that converts glucose (a type of sugar found in most carbohydrates) to ribose-5-phosphate, a form of vitamin B2. Ribose-5-phosphate is an important component of nucleotides, which are the building blocks of DNA and its chemical cousin RNA.
Factors such as infections, certain drugs, and ingesting fava beans can increase the levels of reactive oxygen species, causing the destruction of red

blood cells (they undergo hemolysis faster than the body can replace them. This loss of red blood cells causes the signs and symptoms of hemolytic anemia, which is a characteristic feature of G6PD deficiency). Oxidative stress and inflammation associated with G6PD deficiency may contribute to immune dysregulation. This dysregulation can potentially lead to an overactive immune response, which is a characteristic feature of autoimmune diseases.
Also, healthy red blood cells can produce cholesterol sulfate. If you have low NADPH and/or G6PD variants and your RBC are dying prematurely it will negatively impact cholesterol sulfation production.
ALA and ribose can be beneficial with G6PD SNPs.
When we see G6PD pathway variants, think about increased need for NADPH and increased need for ribose, vitamin B1 (in the form of benfotiamine or allithiamine) and B2 in the form of R5P
Avoid fava beans.
FTL - provides instructions for making the ferritin light chain. Ferritin is the major intracellular iron storage protein. Each ferritin molecule can hold as many as 4,500 iron atoms. This storage capacity allows ferritin to regulate the amount of iron in cells and tissues. Iron is needed for the body to produce red blood cells. SNPs may affect the rates of iron uptake and release in different tissues.
HMOX2 - Homozygous variants in the HMOX2 SNP (even non-clinically validated) have been associated with increased oxidative stress due to the decreased activity of the Heme oxygenase 2 enzyme. Heme, if not properly broken down, can generate harmful reactive oxygen species (ROS) that can damage cellular components, such as DNA, proteins, and lipids. The decreased breakdown of heme by HMOX2 may lead to an accumulation of heme, which may increase oxidative stress and contribute to the development of various health conditions.
POR – This gene encodes the cytochrome P450 oxidoreductase that is required for the normal functioning of the other Cytochrome P450 phase 1 liver detox pathway enzymes. Cytochrome P450 enzymes are responsible for synthesizing cholesterol and steroid hormones, as well as metabolizing medications and other ingested substances. Variants in the POR gene will affect how your other cytochrome p450 enzymes function, and more than 50 SNPs have been known to cause Cytochrome P450 oxidoreductase deficiency, a condition that causes hormonal changes, and skeletal issues.

Recommendations to support Iron regulation and Utilization:

Fenton Reaction recommendations

Hydrogen Peroxide

Background Information-

Hydrogen Peroxide

Your Genes:

GPX genes (glutathione peroxidase) - Involved with reducing hydrogen peroxide into water and oxygen with the help of catalase, to prevent the formation of the highly damaging hydroxyl radical, formed by reaction of the H2O2 with the Fenton Reaction (improperly used iron and copper). Nrf2 is critical for glutathione utilization with GPX variants. Glutathione peroxidase is one of the most important antioxidant enzymes in humans, important for neutralizing many oxidative species including peroxynitrite, using glutathione as a substrate. Also, selenium is required for glutathione to work. SNPs in these GPX genes can lead to altered enzyme activity, stability, or expression, which may affect an individual's susceptibility to various diseases associated with oxidative stress, such as cardiovascular diseases, cancer, and neurodegenerative disorders

GPX1 - GPX1 is a cytosolic enzyme that helps detoxify hydrogen peroxide and lipid peroxides. SNPs in the GPX1 gene can affect enzyme activity, potentially altering an individual's ability to counteract oxidative stress.

GPX4 - GPX4 is unique because it can reduce lipid hydroperoxides within cell membranes and is involved in protecting against oxidative damage to cell structures.

SNP impact: SNPs in GPX4 can affect its function, potentially influencing cell membrane integrity and susceptibility to diseases related to lipid peroxidation. Upregulation of GPX4 can inhibit the accumulation of iron, suppressing ferroptosis in cancer suppression.

GPX4 C718T - You may be at a higher risk for cerebral stroke if you have essential hypertension based on this study. - selenium supplementation

may help to decrease DNA damage. It is recommended not to exceed 400mcg daily.
GPX6 - GPX6 is relatively less studied, and its exact function is not well-defined. The impact of SNPs on GPX6 function remains less clear due to limited research on this isoform.
TXNRD2 - This gene encodes a mitochondrial form important for scavenging reactive oxygen species in mitochondria. May play a role in redox-regulated cell signaling.

Support for Hydrogen Peroxide-

Hydrogen Peroxide Recommendations

NOS Uncoupling

Nitric Oxide

Background Information-

Nitric Oxide and NOS Uncoupling

Your Genes:

NOS1 - (neuronal NOS) NOS1 seems to be the "bad apple of the group" and is more susceptible to creating problems - oxidative and nitrosative stress in the cells and body. NO gets pegged as the problem, and in most cases it is not. It is actually the uncoupled NOS that creates the peroxynitrite that causes most of the problems. SNPs in the NOS1 gene have been associated with various cardiovascular conditions. NOS1-derived nitric oxide is involved in regulating vascular tone and neural control of blood vessels. Genetic variations in NOS1 may influence the production and activity of nitric oxide, affecting vasodilation and blood flow regulation. Some studies suggest that specific NOS1 polymorphisms may be associated with an increased risk of hypertension, atherosclerosis, and other vascular disorders, which can indirectly contribute to venous insufficiency.
SLCL7A's – This enzyme is involved in arginine transport. Arginine is a precursor for the synthesis of nitric oxide (NO) by nitric oxide synthases (NOS). Proper production and functioning of NOS depends on adequate intracellular arginine levels. Low levels of intracellular arginine can lead to

NOS using oxygen instead of arginine, resulting in the production of superoxide (O2−) instead of nitric oxide (NO). More research needs to be done on this gene to understand its function.

To support NO production and minimize peroxynitrite damage:

Nitric Oxide Recommendations

Food, Gut, Histamine, Oxalates

Food and Gut

Food and Gut Background Document

Your Genes:

HLA - The human leukocyte antigen (HLA) system is a complex group of genes involved in the regulation of the immune system. HLA proteins play a crucial role in the recognition of foreign substances (antigens) by the immune system and are essential for immune responses against infections, transplantation, and autoimmunity. The HLA-DQ genes are a subset of the larger HLA complex that encodes proteins responsible for presenting antigens to the immune system, initiating immune responses against pathogens, and modulating the immune system's activity. HLA-DQ proteins are crucial for immune response regulation and are involved in various autoimmune conditions and disease susceptibilities, as well as defense against various infections. They are well known for influencing our risk of developing autoimmune diseases because variants can cause HLA receptors to mistakenly flag peanuts and other things (including our own tissue) as dangerous. The disorder individuals are most predisposed to with variants in their HLA genes is Celiac, an autoimmune disorder characterized by an abnormal immune response to gluten, a protein found in wheat, barley, and rye.
HLA genes are also associated with gluten sensitivity, regardless of celiac. This gene does not determine gluten sensitivity, but it may indirectly affect

the risk of developing it through its impact on immune function. If you want to know if you are reactive, there is a test called the Wheat Zoomer.
Certain HLA variants are also associated with mold sensitivity. You can find these if you do an internet search for HLA-DRA or Dr. Shoemaker, but much of what you'll find discusses testing for that gene (which I do not agree with only testing for single genes), but maybe these people have financial interest in there being a correlation.
However, a study published in the journal PLoS One in 2013 looked at the association between genetic variants in the HLA region and mold sensitivity in a group of individuals with chronic rhinosinusitis. The authors found that certain HLA genes were significantly associated with mold sensitivity.
Note: You may want to consider if dairy is inflammatory for you, as gluten and dairy sensitivity usually are found together due to molecular mimicry.

HLA-DQ2.2- The presence of the HLA-DQ2.2 Haplotype is somewhat associated with susceptibility to Celiac Disease, however it carries less of a risk for Celiac predisposition than other HLA-DQ genes.

HLA-DQA2 - Variants in this gene are also associated with susceptibility for Rheumatoid arthritis. **HLA-DQA2** (rs2858331) - Studies have found an association between the HLA-DQA2 rs2858331 SNP and an increased risk of developing Hashimoto's thyroiditis. When combined with FUT2, there can be an increased predisposition for autoimmune issues.

HLA-DRA - Some studies have suggested that the HLA-DRA rs7192 variant is associated with increased susceptibility to certain autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis, while other studies have found no significant association. This variant is also associated with peanut allergies.

Support for HLA, and Preventing/Lessening severity of Autoimmune conditions:

HLA and Autoimmune Conditions Recommendations

Histamine-

Histamine Background Document

Your Genes:

ABP1 - This gene makes an enzyme called diamine oxidase that degrades histamine. This enzyme is made in the gut so regardless of genetics, if your gut health is suboptimal, you may not make adequate levels of diamine oxidase, increasing likelihood for histamine intolerance. Certain SNPs in this gene may also cause sensitivity to NSAIDs.
MAOA and MAOB - Monoamine Oxidases A and B (MAOA and MAOB) are enzymes involved with degrading amines - histamine, dopamine, and other catecholamines, as well as estrogen. MAOA helps to break down serotonin and dopamine as well, so all these substances may have sluggish clearance if variants are present. HNMT and the MAOs are dependent upon methylation ability, so if you have any methylation issues, it will be like you have a genetic variant and the enzyme won't work as efficiently since it doesn't have the 'fuel' that it needs to do its job. Estrogen inhibits MAO activity, so the age related decline in estrogen may increase MAOB activity. Chronic stress upregulates MAOB activity, as does alcohol.
MAOA and MAOB are the next steps in clearing histamine after HNMT. Variants here will impair our ability to clear histamine. Variants here can reduce efficiency of amine degradation and lead to higher levels of these amines. Vitamin B2 is a cofactor for the MAO enzyme to work, and the byproducts of this reaction are hydrogen peroxide and ammonia. High stress reduces the activity of MAO enzymes, causing higher amine levels MAOB is the main enzyme for the breakdown of phenethylamine (PEA) and histamine.
NOTE: The MAOB gene is located on the X chromosome. In males who have one X chromosome and one Y chromosome (XY), they will inherit only one copy of the MAOB gene because they have only one X chromosome, and if it is variated, it may cause the effect of being like it is homozygous.

Support for Histamine-

Histamine Recommendations

Nrf2 KEAP1

Background Information-

Nrf2/KEAP1 Background Document

Your Genes:

NFE2L2 - The NFE2L2 gene is responsible for encoding a protein (making) called NRF2, which controls so many processes in the body. NRF2 is responsible for activating many of your other genes that produce detox proteins (like glutathione and NADPH), detoxification enzymes, and others involved in inflammation, injury, and elimination of free radicals. Nrf2 is a major protector against oxidative stress and iron dysregulation, it influences autophagy, and is necessary for the enzymes that reduce H2O2. NFE2L2 also activates the production of glutathione, as well as its recycling.
We need NADPH for the activation and function of Nrf2. NFE2L2 also activates the production of glutathione. Even if someone has perfect Nrf2 genes, ochratoxin or aspergillus exposure or other toxins will override NFE2L2 and can still inhibit Nrf2 activity.
Nrf2 related genes are inhibited by mold mycotoxins - Even if someone has perfect Nrf2 genes, ochratoxin or aspergillus exposure or other toxins will override NFE2L2 and can still inhibit Nrf2 activity.
Certain genetic variations of NFE2L2 can reduce the expression and activity of NRF2; in turn, lower NRF2 expression may prevent the body from detoxing compounds that cause oxidative stress.

KEAP1 - Because it has a major influence on things like iron sequestration, Nfr2L2 and KEAP1 variants will override everything else related to iron.

KEAP1 - UPREGULATION- The KEAP1 variant rs9676881 is an upregulation of the enzyme activity and can cause you to hold more tightly onto your Nrf2, so you don't release as much of it to fight oxidative stress. In turn, because it holds onto Nrf2, it has a major influence on things like regulating iron sequestration.

Cruciferous veggies, garlic, and rosmarinic acid can help with KEAP1 upregulation.

Support for Nrf2-

Nrf2/KEAP1 Recommendations

NAD+ NADPH

Background Information-

NAD/NADPH Background Document

Your Genes:

IDO1 & IDO2 - IDO plays an important role in modulating T-cell behavior (T cells play a crucial role in the immune response by recognizing and eliminating foreign invaders, but when they become overactive or fail to regulate themselves properly, they can mistakenly attack the body's own cells and tissues) by controlling the amount of tryptophan available. The dysfunction of certain immune cells, including T cells and natural killer (NK) cells, can indeed contribute to the development of autoimmunity.
IDO1 and IDO2 are involved in conversion of tryptophan to kynurenine. SNPs are gain of function SNPs that will upregulate tryptophan through the kynurenine pathway (an important immune-modulating pathway), making the brain-inflaming quinolinic acid, but then hopefully moving straight on to producing NAD, because if quinolinic acid builds up to high levels, it can cause lipid peroxidation (oxidative stress), leading to neurotoxicity and brain inflammation, anxiety, sleeplessness, etc, and increasing potential for depression.
A suppressed immune system can also increase the risk of opportunistic bacterial, fungal, parasitic, viral infections and cancer.
Vitamin A can help to balance IDO activity and support production of T cells and NK cells. Also, cruciferous veggies!
NADSYN1 - NAD synthetase (NADSYN1) catalyzes the final step in the biosynthesis of NAD from nicotinic acid adenine dinucleotide. Supporting Nrf2 is an essential part of supporting NADSYN1.

Suggested Recommendations:

- NAD Gold or NAD+ Platinum by Quicksilver Scientific
- Resveracel or Niacel by Thorne
- Molecular hydrogen

Support for NAD+ and NADPH-

NAD/NADPH Recommendations

Glutathione	Antioxidant and Detoxification Agent

Background Information-

Glutathione Background Document

Your Genes:

CBS - Cystathionine Beta Synthase (CBS) sits at the intersection of whether homocysteine gets recycled back into SAMe to drive methylation, or if it gets sent down the transsulfuration pathway to profive sulfur groups for detoxification, as well as the important job of making glutathione.
CBS is responsible for converting homocysteine to cystathionine, the first step in the transsulfuration pathway that ultimately produces glutathione (the master antioxidant). This gene also plays a role in metabolism of sulfur. With the help of vitamin B6, the CBS enzyme is responsible for removing excess sulfur containing amino acids from the pathway. If excess sulfur-containing amino acids, like homocysteine, were to accumulate in the body, it could lead to health issues such as cardiovascular problems, oxidative stress, and potential damage to blood vessels. Proper sulfur metabolism is crucial for various biological processes and is fundamental for maintaining a healthy body.
Some CBS polymorphisms create an upregulation, potentially causing homocysteine to rush down the transsulfuration pathway at up to 10 times faster than without the variant. Conversion impairments prevent homocysteine from being properly used, creating low homocysteine,

diminished glutathione levels, and excesses in ammonia (a by-product of amino acid metabolism), sulfites and sulfates.
Some variants are upregulations and others are downregulations, meaning that some variants speed up enzyme activity and others slow down activity, so conceivably, having multiple variants could cancel each other out. If you are curious as to what your methylation status is, including your homocysteine levels, and where wrenches in the methylation/transsulfuration pathway are, you can order a Methylation Plasma profile (Doctor's Data or Genova).
Suspect CBS dysregulation and/or depleted B6 in those with:

- Sulfur sensitive
- Sulfa drug sensitive
- High homocysteine
- Low glutathione
- High ammonia
- High oxalates (indicated by OAT test)

CBS heterozygous variants can affect homocysteine's ability to get converted into glutathione. CBS variants also increase sulfite levels in the body, which need to be converted to sulfate (via the SUOX enzyme, of which yours has zero SNPs 🙂).
Homozygous C699T variant carriers have been associated with increased lowering of homocysteine, as these variants are thought to be upregulations (however, yours has been slightly elevated). Overall, the consequences of this variant remain debated as some believe it leads to an upregulation of the CBS gene, whereas many others believe there is not enough evidence to draw that conclusion.
CBS A13637G (rs2851391) - You are heterozygous - The variant at this position in the CBS gene has been associated with an increased risk for cleft lip with or without cleft palate (CLP) in infants when mothers had low folate intake. The variant at this position in the CBS gene has been associated with an increased risk for spina bifida. This variant was associated with a 57% reduction of failure risk in folate treatment for hyperhomocysteinemia. Additionally, 33% of this effect was mediated by baseline CBS promoter methylation. The variant at this position in the CBS gene has also been associated with total plasma homocysteine concentrations.

Some recommendations for supporting CBS are taurine (or in the magnesium taurate form), vitamin B6, and liposomal or S-Acetyl-glutathione.

GCLC - The GCLC and GLCM genes use ATP and glutamate to make the glutathione molecule, and mold/mycotoxins and infections reduce this gene's function.

I'd recommend liposomal or S-acetyl glutathione forms instead.

GSS - GSS is the final step where you take the three amino acids and assemble them to create glutathione. If there are lots of 2's very inflamed. GSSG is oxidized glutathione and requires NADPH to recycle back into reduced GSH.

If people with SNPs are given more NAC or glutamine, they often will backfire and glutamate goes up because the body can't use it. ATP is a cofactor for GSS, so Krebs problems can cause trouble making Glutathione even if GSS is fine. NRf2 is needed for the GSS enzyme to work.

Variants in GCLM & GCLC, and GSS will significantly impact the ability to assemble the glutathione molecule, affecting glutathione levels. In this case, NAC is not going to be the way for you to boost glutathione in the body. The GCLC and GLCM genes use ATP and glutamate to make the glutathione molecule, and mold/mycotoxins and infections reduce this gene's function.

I'd recommend liposomal or S-acetyl glutathione forms instead.

GST genes- The GSTs are what take glutathione from being an antioxidant to a detoxification substance. Variations in this gene can change an individual's susceptibility to toxins. It's important to note that although each GST gene may have its own unique properties, there is also functional redundancy among the GST genes. This redundancy allows for the compensation of enzyme activity when one GST gene is not functioning optimally or absent, ensuring the overall detoxification capacity of the body is not compromised. Each GST gene may exhibit varying substrate specificity, meaning they may have preferences for different types of chemicals or compounds.

> **GSTA** genes are the most important for detoxing carcinogens, therapeutic drugs, environmental toxins, and products of oxidative stress. In regards to mold and mycotoxins, glutathione conjugation only plays a role in aflatoxin and ochratoxin (aspergillus exposure) that we are aware of. The two most significant GST variants for these two

mycotoxins are GSTA and GSTM. These may also inhibit the clearance of estrogen.

GSTO1 - More research needs to be done on this gene to understand its function.

GSTZ1- More research needs to be done on this gene to understand its function.

Supporting GST SNPs through nutrition involves providing adequate levels of certain nutrients that can help optimize the enzyme's function. While specific recommendations may vary based on individual genetic variations and overall health status, the following nutrients are generally considered important for supporting GST activity:

- I recommend liposomal glutathione or S-acetyl-glutathione forms. Also consuming foods rich in glutathione precursors like sulfur-containing amino acids (cysteine, methionine) and antioxidant-rich foods (fruits and vegetables) may help support optimal glutathione levels.
- Antioxidants are involved in neutralizing reactive oxygen species (ROS) and can be influenced by oxidative stress. Consuming a diet rich in antioxidants, such as vitamins C and E, beta-carotene, and flavonoids, may help reduce oxidative stress and support GST activity.
- When we see variants on GSTs or NRF2, we want to think about cruciferous veggies, DIM, garlic, rosmarinic acid to help with that upregulation.
- Also, alpha lipoic acid, artichoke (a great bitter that helps move bile!), curcumin, folate, magnesium, and milk thistle help to modulate GST activity
- Selenium is a cofactor for GST enzymes. Including selenium-rich foods in the diet, such as Brazil nuts, fish, and eggs, may support the activity
- B-vitamins: Certain B-vitamins, such as folate (B9), vitamin B6, and vitamin B12, are involved in various cellular processes, including DNA repair and synthesis. Adequate levels of these vitamins may support optimal GST function.
- Also, supporting Nrf2 helps support the GSTM gene (see recommendations in Nrf2 section).
- With GST variants, first support phase 3 detox- ensuring daily elimination, then support bile flow to ensure we are getting toxins out

of hepatic cells and into excretion pathways, THEN we can think about GST support, depending on how sensitive you are. Either way, you definitely want a binder on board. Then think about straight glutathione support. If you are sensitive, start with broccoli sprouts and cruciferous veggies before doing more targeted supplements

GSR - This is involved with the recycling of glutathione, by using NADPH as an electron donor, so that it can keep acting as a free radical neutralizer. Variants here can cause glutathione to get stuck in its oxidized form and not be able to recycle back to the reduced form (loaded and ready to work), not only creating low glutathione levels, but oxidative stress due to higher levels of oxidized glutathione.

Keep in mind Nrf2 regulates GSR activity, so this may be further compromised if you have variants in either of these areas.

Recommended Support for glutathione recycling

- Nicotinamide riboside is a phenomenal way to support NAD+ production and glutathione recycling.
- Vitamin B2/Riboflavin (R5P), selenium, zinc, magnesium, flavonoids, carotenoids, and vitamins C and E are some of the minerals, plant compounds, and vitamins that can help to recycle glutathione. Parsley has lots of health benefits, including assisting in the recycling process.
- Alpha lipoic acid and grape seed extract
- Quicksilver Scientific's NAD Gold
- Use of molecular hydrogen in almost all those cases for additional redox support
- You can support the functioning of both of these through supporting Nrf2 levels
- Grape seed extract helps to convert quinolinic acid into NAD+.
- Pulse glutathione with caution because GSR variants may not allow glutathione to be reduced. Can cause more inflammation if it can't be recycled.
- There is a product called GSR Assist that has many of these ingredients all rolled into one bottle. Contact me if you want to order, as it has to be ordered by a practitioner (and drop shipped to your house).

Support for Glutathione-

Glutathione Recommendations

FOXO

Background Information-

FOXO

Your Genes:

FOXO6 – Longevity genes, dependent upon NAD+. FOXO6 is involved in various biological processes, including glucose metabolism, oxidative stress response, and neuronal development. It is particularly noted for its role in the brain, where it affects memory and cognitive functions. SNPs can affect memory, learning, neurodegenerative diseases, metabolic disorders, and tumor suppression/cancer response.

Sulfation

Background Information-

Sulfation Background Document

Your Genes:

CHST genes - Carbohydrate Sulfotransferases. Variations in the CHST gene family can affect sulfate levels and sulfation ability in a variety of ways, which can have implications for a range of physiological processes and health outcomes. The CHST (carbohydrate sulfotransferase) gene family includes several members that encode enzymes responsible for sulfation, a process that involves adding sulfate groups to various molecules in the body. This process is important for a variety of physiological processes, including the

regulation of cell signaling, the metabolism of hormones and neurotransmitters, and the maintenance of the extracellular matrix.
SLC26A6 - SLC26A6 is an angiotensin activated signaling pathway, bicarbonate transport, cellular response to fructose stimulus, oxalate transport and sulfate transport.
SLCO - Involved with transport of bile acids, hormones, bilirubin, various xenobiotics, and drugs from the blood to liver cells to be cleared by the body. Variants can increase potential for tissue accumulation of toxins, and keep toxins from getting into liver cells to then be detoxified. SLCO genes pull toxins from the bloodstream or from where they are sequestered, into hepatic cells for detoxification. With variants, we may see more circulating toxins in the bloodstream. With ongoing exposure, we will see much more storage and often people will have a difficult time building muscle because the body will preferentially store fat as a protective mechanism and burn muscle for fuel instead. Lack of bile is a BIG driver of constipation.
SLCO2B1 - The limited available evidence suggests that they may modulate the transport of sulfate conjugates and impact the sulfation of certain endogenous compounds, including estrogens and DHEA metabolites.

Support for Sulfation-

Sulfation Recommendations

Glucuronidation

Background Information-

Glucuronidation Background Document

Your Genes:

PGM2 - SNPs in the PGM2 gene can affect glucuronidation by altering the activity and expression of UDP-glucuronosyltransferases (UGTs), which are enzymes responsible for glucuronidation. The PGM2 gene encodes for phosphoglucomutase 2 (PGM2), an enzyme involved in the biosynthesis of UDP-glucuronic acid, which is a substrate for UGTs. UDP-glucuronic acid is essential for glucuronidation, which is a process that converts lipophilic

compounds, such as drugs, toxins, and endogenous compounds, into more water-soluble metabolites that can be excreted from the body. Glucuronidation plays a crucial role in drug metabolism, as it can affect the bioavailability, efficacy, and toxicity of drugs.
Some studies have suggested that certain SNPs in the PGM2 gene can affect glucuronidation by altering the activity and expression of UGTs. For example, a PGM2 gene variant (rs4977756) has been associated with decreased expression of UGT1A1 in the liver, which can affect the metabolism of drugs such as irinotecan and bilirubin. Other PGM2 SNPs have also been linked to altered glucuronidation of drugs such as zidovudine, tamoxifen, and paracetamol. However, the exact mechanisms by which PGM2 SNPs affect glucuronidation are still not well understood and require further research.

Support for Glucuronidation-

Glucuronidation Recommendations

Acetylation

Background Information-

Acetylation Background Document

Your Genes:

PANK genes -There are 4 PANK genes, with PANK1-3 encoding for the enzymes called pantothenate kinases, which are crucial for the synthesis of coenzyme A (CoA) from pantothenic acid. There is also PANK4, which encodes a phosphatase that regulates CoA synthesis. Single nucleotide polymorphisms (SNPs) in the PANK genes can potentially impact health, detoxification processes, and the metabolism of vitamin B5 (pantothenic acid) which is used in the synthesis of CoA. CoA is a fundamental coenzyme involved in various cellular processes, including energy metabolism and the synthesis of fatty acids and other important compounds. CoA is involved in various cellular processes, including detoxification and metabolism of vitamin B5. SNPs can have several effects:

- Impaired CoA synthesis - Coenzyme A is essential for various metabolic reactions, including the breakdown of fatty acids, the production of energy, and the detoxification of certain substances. SNPs in PANK genes may disrupt coenzyme A synthesis, leading to decreased levels of CoA and potentially affecting these metabolic processes.
- Impacted detoxification: Coenzyme A plays a role in the detoxification of xenobiotics (foreign substances) through conjugation reactions. Altered PANK genes function due to SNPs may hinder the detoxification process, potentially affecting the body's ability to eliminate toxins efficiently.
- Vitamin B5 metabolism: Pantothenic acid is a precursor to CoA synthesis. SNPs in PANK genes could influence the efficiency of converting pantothenic acid into CoA, potentially affecting the availability of CoA for different biochemical reactions in the body. This, in turn, might have implications for overall vitamin B5 metabolism.

PANK3 - This PANK enzyme is more sensitive to regulation by CoA itself. More information is needed on PANK3 to understand the effects of the mutations in this enzyme, however it is most expressed in the liver.

Support for Acetylation-

Acetylation Recommendations

Fats, Carbs, Proteins, Vit A, & Vit D	Fats/Bile

Fats, Carbs, Proteins, and Bile

Fats, Carbs, Proteins, and Bile Background Document

Your Genes:

ELOVL2 - Involved with transforming fatty acids to longer-chain fats - EPA to DHA. The ELOVL2 gene encodes an enzyme involved in fatty acid elongation. Genetic variations in these genes can impact the elongation of

omega-3 fatty acids, which is necessary for the production of some PRMs. Genetic variations in the ELOVL2 gene may influence the efficiency of the EPA to DHA conversion process. Some individuals may have genetic variants that result in reduced conversion rates, leading to lower DHA levels despite adequate EPA intake.

Consuming DHA directly through dietary sources or supplementation may be beneficial. If you are curious to what your fatty acids are doing, you can do something like an Omega Quant test.

I recommend getting a fish oil that has a higher amount of DHA than EPA. This is why I recommended OmegaGenics Neuro 1000 for you in your Fullscript recommendations.

ABC Genes - A family of genes that encode for proteins that are involved in the transport of a variety of different molecules, including bile acids, across cell membranes. There are several ABC transporters that are specifically involved in bile acid transport, including ABCG5/G8, ABCB4, and ABCC2. Genetic variations in these ABC transporters can impact the transport of bile acids across cell membranes and thus affect the physiological processes that involve bile acids. SNPs here can affect lipid and glucose metabolism, as well as drug and xenobiotic detoxification.

Regulated by Nrf2. People with antiporter and exporter issues such as SLCO and ABCC are more vulnerable to toxin bioaccumulation, same with PON1 variants.

Variants cause impaired bile excretion. ABC variants are associated with high potential for retained toxins. Ensuring bile is flowing will support mobilization of toxins from liver to the gut. Growing body of evidence that there may be tissue retention of glyphosate.

ABCB genes often encode multidrug resistance proteins, which are involved in cellular drug and xenobiotic transportation, but do not have a direct link to bile

ABCB4 - ABCB4 is more directly involved in bile transport. Variants can result in decreased bile flow and lead to bile related conditions like intrahepatic cholestasis.

ABCB11 - Plays a significant role in transporting bile salts, which are essential for the digestion and absorption of dietary fats, from the liver into the bile. Genetic variations in the ABCB11 gene can result in impaired function of bile salt export pump, leading to impaired bile acid excretion and retention of bile acids within hepatocytes. This can

lead to liver diseases and forms of cholestasis. These conditions can manifest with symptoms like jaundice, itching, and occasionally nausea.

ABCC genes contribute to bile synthesis, utilization, or transport processes, and dysregulation or genetic variations in these genes can result in bile-related disorders or impaired bilirubin elimination. ABCC genes encode multidrug resistance-associated proteins that participate in the efflux of various substances, including drugs and endogenous compounds, but do not have an exclusive focus on bile-related processes. Some members of the ABCC gene family are involved in bile synthesis, utilization, or transport.

ABCC2 - Plays a significant role in transporting conjugated toxins (from Phase 2 Detoxification) and other molecules from the liver into the bile. ABCC2 SNPs have been associated with alterations in bile acid transportation in the liver, resulting in altered bile formation and biliary flow, and they have been linked to several diseases, including drug-induced liver injury, and intrahepatic cholestasis of pregnancy. Also plays a part in the elimination of bilirubin, a waste product derived from the breakdown of hemoglobin. Associated with nausea and jaundice

ABCC3 - ABCC3, also known as MRP3, is involved in the transport of certain bile acids and other organic anions.

ABCC4 - ABCC4, also known as MRP4, is implicated in the transport of prostaglandins and other endogenous compounds involved in bile formation and regulation.

Recommendations for Fats, Carbs, Proteins, and Bile:

Fats, Carbs, Protein, and Bile Recommendations

Neurotransmitters and BH4	

Background Information-

Neurotransmitters and BH4 Background Document

Your Genes:

OXTR - This is your Oxytocin receptor gene - Oxytocin is called the “Bonding hormone.” Out of all the genes in the software I use, this gene is the most predictive in terms of personality.
With variants, we see overexpression of oxytocin, deeper connections with people, more charitable giving, more sensitive parenting techniques, and being more sensitive in general. The biggest takeaway for SNPs in this gene is a need for creating healthy boundaries to prevent yourself from being a “pushover” and/or absorbing other people’s negative energies.
For individuals with homozygous variants in OXTR, they will be much more in tune with energy from other people. This can make them more prone to nervous system dysregulation, because they are not only dealing with their own energy and nervous system, but what everyone else is throwing at them. This may cause these individuals to socially isolate because they get so easily stimulated by other people. Women with OXTR homozygous variants can get stuck in abusive relationships, deeply connecting and bonding with people whether or not they should be because they "find the good things" in the abuser. People that don't have these variants will tend to emotionally "dump" all their stuff onto these people.
Studies have shown that individuals with the GG genotypes (which you have) are more empathetic, can become more attached, feel less lonely, have a decreased level of sociality, employ more sensitive parenting techniques, and have lower rates of autism.

Mitochondria Function	

Background Information-

Mitochondria Function Background Document

Your Genes:

NDUF genes - The NDUF genes, specifically NDUFAB1, NDUFB8, NDUFB9, and NDUFB10, are part of a larger group of genes known as NADH dehydrogenase (ubiquinone) genes. These genes play a key role in the mitochondrial electron transport chain that makes ATP (cellular energy). ATP is the primary energy source for cellular activities.
In general, SNPs in NDUF genes can contribute to mitochondrial dysfunction, impairing energy production and cellular health, and potentially leading to various health conditions. Mitochondrial disorders, often arising from genetic variants in mitochondrial genes, can manifest as a range of symptoms affecting multiple organ systems, including the nervous system, skeletal muscles, heart, and others. These disorders may present as muscular weakness, neurological problems, metabolic abnormalities, or a combination of symptoms.
In relation to fertility, the connection between NDUF genes and fertility lies in the essential role of mitochondrial function in reproductive health. Mitochondrial dysfunction can lead to increased production of reactive oxygen species (leading to oxidative stress). Proper mitochondrial function is crucial for energy production, which is vital for several aspects of fertility, including gametogenesis, fertilization, and early embryonic development. In females, oocyte maturation and quality are highly dependent on mitochondrial energy production. Variants in NDUF genes can compromise the energy supply to the developing embryo, leading to developmental arrest or pregnancy loss. Antioxidant therapy to reduce oxidative stress and mitochondrial replacement techniques are potential areas of therapeutic research.

Support for Mitochondria function-

Mitochondrial Function Recommendations

Phase I + CYP	

Background Information-

Phase I and CYP Background Document

Your Genes:

CYP3A5 - The CYP3A5 gene encodes a member of the cytochrome P450 superfamily of enzymes. CYP3A5 metabolizes drugs as well as the steroid hormones testosterone and progesterone. One study found that a common polymorphism in the CYP3A5 gene (rs776746) was associated with lower levels of progesterone and increased risk of pregnancy loss (you have a heterozygous SNP here). Another study found that variations in the CYP3A5 gene were associated with differences in the responsiveness to progesterone treatment in women with infertility.
CYP3A7 - CYP3A7 is primarily expressed in fetal and neonatal liver and is responsible for metabolizing certain compounds. While CYP3A7 has a limited role in adults, it is more active during fetal development and in neonates. Its activity declines as individuals grow and mature, and CYP3A4 becomes the primary enzyme responsible for metabolizing various substances in the adult body.
CYP4A11 - is involved in the balance of lipids in the liver, however this gene is typically highly variable [ref]. If this enzyme is up-regulated, you may be more likely to develop nonalcoholic fatty liver disease in response to ROS [ref].
CYP51A1 - involved in cholesterol biosynthesis and plays a role in sterol metabolism and plays a key role in the biosynthesis of cholesterol. This process is essential for the production of cholesterol, which is a vital component of cell membranes and serves as a precursor for the synthesis of steroid hormones, bile acids, and vitamin D. This SNP may be associated with altered glycemic HbA1c levels, and is typically high.

Support for Phase I and CYP issues-

Phase I and CYP Recommendations

PON1	

Background Information-

PON1 Background Document

Your Genes:

PON1 acts as an antioxidant and requires calcium to work. **Variants in this gene can impair the body's ability to clear pesticides (including glyphosate/Roundup), which can then bioaccumulate in the body.** Also, the PON1 gene (paraoxonase 1) is involved in the metabolism of cholesterol and is an antioxidant enzyme that is primarily synthesized and secreted by the liver.
PON1 plays an important role in the metabolism of high-density lipoprotein (HDL) cholesterol, which is considered "good" cholesterol as it helps to remove excess cholesterol from the bloodstream and reduce the risk of cardiovascular disease. In addition to facilitating the formation of HDL cholesterol, PON1 also plays a role in protecting against the oxidation of LDL cholesterol, which is a key step in the development of atherosclerosis. Polymorphisms in the PON1 gene can affect the activity of the enzyme and, consequently, HDL metabolism and cholesterol levels.
Buy organic, use a good water purification system and remineralize. Polyphenols (including anthocyanins and flavonoids) found in fruits and vegetables have been shown to increase HDL levels. Pomegranate, astaxanthin, and quercetin have shown to support PON1 activity.

Support for PON1-

PON1 Recommendations

Nutrient Metabolism

Nutrient Metabolism Background Document

SELENOS - SELENOS encodes for selenoprotein S (SEPS1) which has an important role in endoplasmic reticulum (ER) stress responses, and

inflammation control; however, as a selenoprotein, this selenium-containing oxidoreductase also breaks down hydrogen peroxide, and peroxides. Suppression of SELENOS in macrophages has been shown to increase IL-6 and TNFa. SNPs in this gene have been associated with altered cytokine levels, and variable outcomes dependent on selenium status.

MTHFR, Folate, and Methylation

Background Information-

MTHFR, Folate, and Methylation Background Document

Your Genes:

MTR - methionine synthase - uses methylfolate to convert homocysteine back to methionine in order to make SAMe, the universal methyl donor. It also works with MTRR to use SAM to convert cobalamin into methylcobalamin. *MTR requires vitamin B12 and zinc to work*. If oxidative stress is low, MTR functions well and the methylation cycle recycles homocysteine back into SAM. If, on the other hand, oxidative stress is high, MTR does not function well and CBS is stimulated. The CBS enzyme then uses homocysteine to start the process of making glutathione. Some things that hinder MTR activity include: insufficient protein, consumption of rancid oils, heavy metals, and anything that increases demand for glutathione. Methylcobalamin (B12) can support MTR functioning.

DHFR - Variants inhibit folic acid metabolization in the body, as DHFR is involved in 2 of the 5 steps of converting folic acid into methylfolate (using NADPH as a cofactor). Too much synthetic folic acid can overwhelm the DHFR enzyme and cause blood levels of unmetabolized folic acid to rise, which is undesirable because rising synthetic folic acid levels block folate receptors and reduce the ability of natural food folates to bind to them. So essentially, folic acid may cause further folate deficiencies because it can ‘gum up’ the folate pathways that allow it to get into the brain.

DHFR works with MTHFR → folate can't do its job effectively when there are DHFR variants. The DHFR enzyme has another really essential role in converting BH2 back into BH4, a vital cofactor involved in making nitric oxide, serotonin and dopamine, and neutralizing ammonia. It also helps prevent NOS uncoupling and excess superoxide (2 nasty free radicals). Magnesium is a cofactor. Blood sugar issues exacerbate DHFR variants. Ensure adequate B12 levels before supporting with higher doses of forms of folate.

Support for Methylation-

Methylation Recommendations