John Doe

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Recommendations based on DNA results – Please follow only under the advice and care of your physician.

- Minimize caffeine
- Avoid ibuprofen and naproxen regularly and you may need reduced doses of blood thinners if you ever need them
- See handout on CYP2D6 for possible drug sensitivities
- Avoid GMO foods and high oxalate foods if have been using antibiotics or gut needs healing
- Avoid gluten containing foods and supplements. Also consider eliminating dairy and soy
- If cholesterol high, watch cholesterol in foods
- Check RBC folate and homocysteine levels
- Check ammonia and molybdenum levels
- Avoid fluoroquinolones, such as Cipro and Levaquin
- Eat beets, lamb, and spinach as a source of betaine
- Do you have chemical sensitivities to perfume or cigarette smoke? (possible need for SAMe or phosphatidyl choline)
- Do you experience anxiety or panic attacks? (betaine, TMG, check RBC folate levels)
- If sensitivities to sulfur foods, remove for three days, then introduce back in and see how you feel. Ammonia and molybdenum levels can also be checked for a block in sulfur pathway. If sulfur a problem, stay away from oxalate foods and address possible leaky gut.

Supplement Recommendations

- Nattoserrazimes (CYP4V2, ITGB3, NR1I12, F11)
- Phosphatidyl choline (PEMT; if multiple chemical sensitivities)
- Molybdenum (SUOX; check multi vitamin)
- Sam-e (AHCY, MTR/MTRR)
- TMG (BHMT, but check for anxiety because of COMT)
- Quatrefolic (5-MTHF; MTHFR, MTHFD1, MTHFR, MTHFS, MTR/MTRR, PEMT, MAO A)
- Probiotic synergy (FUT2)
- 5-HTP (MAO A)
- PharmaGABA (GAD1)
- Adenosyl B12 (COMT, TCN1/2)
- Cod liver oil (for vitamin A; BCMO1)
- Mitochondrial NRG (NDUFS7)

What You Need to Know

In the world of genetic testing, things can become complicated very quickly. We are beginning to see thousands of patients testing their genetics with the goal of finding answers to their health challenges. Unfortunately, they often times end up being more confused after testing than when they started, or even feel scared or helpless. It doesn't have to be this way.

As physicians, we must understand and explain the genetic science in ways that our patients can understand. If we don't, then things will not improve as a result of genetic testing. In order to understand your genetics and your SNP report, you need to know two key terms – genotype and phenotype.

Genotype

Your genotype includes your unique, individual DNA sequences. It includes all your genes and SNPs found within your genes that you inherited from your parents. This information is found on your 23andMe variant report.

The genotype is nothing more than a categorical list of individual genes and the DNA coding which is unique to you. The colorful variant reports you have received lists whether you inherited the good or bad version of a given gene. However, looking only at the genotype, while ignoring the phenotype, is not a useful approach to treatment. Simply looking at a list of genes and their sequences in isolation, takes them out of context.

We look at your genotype by evaluating SNP's or single nucleotide polymorphisms. This big word is essentially the difference in your DNA coding that makes your body work differently and uniquely as compared to someone else's. Sometimes SNP's will improve your health and sometimes they may worsen it. This report will help you determine which SNP's may be helping or hurting you. The areas where you have the most significant risk are colored red. Yellow areas are an intermediate risk for health concerns and green areas are where your genetics are coding for ideal function.

Within your genotype there can be a combination of SNPs which predispose you to a higher risk of health issues compared to other individuals that do not have this combination of SNPs. For example, many people have genetic variants in MTHFR C677T, COMT, and MAO-A. People with this genetic SNP combination will frequently have high adrenalin, inability to methylate, and experience high anxiety, due to the inability to break down neurotransmitters properly. They may also suffer from mood swings, demonstrate aggressive behavior, have elevated homocysteine levels and be at elevated risk for heart disease and stroke.

Another example of a genotype combination might be someone with SNPs in GAD1, ACE, AGT, ADD1, COMT, MAO, and MTHFR (A1298C). This haplotype causes high stress, neuroinflammation, low gut function, and slow methylation**.**

The ACE, AGT, and ADD1 genes influence levels of angiotensin, which is a stress hormone made by our kidneys. When genetic variants in these genes are present together, the body has elevated levels of angiotensin causing high blood pressure and reduced blood flow to the GI tract. Some studies show these SNPs may even cause damage to the heart valve, since increases in blood pressure and cortisol usually accompany the increase in angiotensin.

GAD1 involves the breakdown of glutamate into GABA, so the more GAD SNPs that are present, the less efficient the body is at making GABA. This can lead to neurologic inflammation since too much glutamate in the brain (think MSG) leads to excess brain activity, seizures, and inflammation. With GAD1, the tendency is towards glutamate and away from GABA, which can lead to neurological symptoms that change behavior, mood, and appetite.

Another genotype combination is COMT and MAO-A SNPs. These individuals will struggle to break down stress hormones like adrenalin and norepinephrine. Individuals with the COMT and MAO haplotypes are usually highly intelligent, driven, and susceptible to burn-out and OCD issues.

If as a physician all you are treating is an individual based on their genotype (the results of individual genes), but ignore the combination of SNPs in their genotype, you are going to have less than satisfactory results. Yet even looking at both the genotype and the genotype combinations will leave you falling short. To really see the big picture, to really take good care of the body and resolve issues, you have to study the genotype, appreciate the genotype combinations, and make sure you understand them!

The bottom line with genotype is that it is impossible to effectively prescribe vitamins or treatment plans based on only this information. Doing so will result in frustration, added expense, and lack of results for you as a patient. To be successful you must also look at the phenotype. This is critical to decide which treatment protocol will be the most effective for you.

Phenotype

The phenotype is the most important part of the genetic puzzle. Simply put, your phenotype is the outward appearance or result of your genotype. The phenotype concerns the named “disease” that medicine uses to label patients – obesity, cancer, metabolic syndrome, diabetes, etc. Your phenotype describes how your inherited

genes become active or expressed through diet, stress, toxins and other life experiences and the result of that expression. The phenotype brings together the concept of genetics with environment to determine what you will experience in your day to day life.

Your phenotype is found by performing a thorough history, taking into account your chief complaint as the patient and evaluating your over-all health. Your phenotype includes your symptoms and the background of how they started. The phenotype is the end result of your genes interacting with your environment. In other words your phenotype represents all of your genetics plus all of the environmental influences – stress, toxins, malnutrition, etc. – and their combined affect on your genetics.

When we try to treat disorders arising from genetics, we must realize that the phenotype is the most important thing – it's the only reason why a patient actually feels sick or has symptoms in the first place. It is the reason the patient goes to the ER or to the doctor's office. The phenotype is what we consciously experience in our bodies – what we would call our level of health and wellness.

For example, you cannot consciously feel your MTHFR gene. But you can feel depressed from the lack of ideal expression of the MTHFR gene and depression is a well-known phenotype. Similarly you can't feel your COMT, ACE or BHMT genes, but you can have gallstones and chronic acid reflux which are also common phenotypes in our society. Having depression, gallstones and/or acid reflux are not genetic problems, they are phenotypes CAUSED by the interaction of your genes and the environment within your body and your digestive system. Said scientifically:

The phenotype is the physiologic expression of haplotypes over time; the epigenetic final result of environment + haplotype (SNP combinations) yielding a particular set of symptoms such as high blood pressure, leaky gut, GB disease, panic/anxiety disorder, etc.

In the end treating genetic problems isn't about following a predetermined formula. It is far from it. Treating you as a patient for genetic issues involves understanding where your physiology is most imbalanced and stressed. The information that is necessary to successfully figure that out requires looking at your genotype and your phenotype together.

Doctors have been helping patients heal for thousands of years, long before we had genetic testing. Your genes are not your destiny, but they are your tendency. Because the world today is more toxic and more stressful than ever, it is placing added stress on our genetic predisposition and this where most problems arise.

This report will be looking into all of these aspects of your genetic coding with the goal of using your individual genetic profile to improve your overall health.

The highlighted genes below show whether you have two (red), one (yellow) or no (green) copies of a variant for one or more SNPs in that particular gene. If the area is highlighted red, it requires the most attention followed by your yellow areas. Green areas are where your body is functioning ideally. The more red or yellow areas you have in a section the greater the potential concern. The more green areas you have in a section, the greater you can feel assured that your body is functioning ideally here.

DETOX - What you need to know

CYP1A1, 1A2, and 1B1 – These genes are involved in metabolizing estrogen and caffeine. Individuals with SNP's in these genes may have high estrogen levels as well as difficulty processing caffeine. In addition these SNP's can cause caffeine to prevent estrogen from being metabolized and broken down leading to estrogen dominant symptoms. These symptoms include bloating, fluid accumulation, weight gain, breast tenderness etc.

Lifestyle recommendations: People with SNP's in this area should be careful with caffeine consumption because it can elevate estrogen levels by 80%. People with known estrogen dominant symptoms or elevated estrogen levels should have these genes checked and will likely need to significantly reduce or avoid caffeine.

In addition, people with SNP's in these genes should consider a complete estrogen metabolism pathway test to make sure they are metabolizing their estrogens into healthy forms (cancer preventative metabolites) vs. unhealthy forms (cancer causing) of estrogen. GMO foods (corn and soy products containing the chemical glyphosate) can cause every gene in this pathway to activate or turn on causing significant problems for individuals with SNPs in these genes.

CYP2E1B, 2E14, 3A4, and 3A43 – These genes are involved in metabolizing estrogen and caffeine. Individuals with SNP's in these genes may have high estrogen levels as well as difficulty processing caffeine. In addition these SNP's can cause caffeine to block estrogen from being metabolized or broken down in the body leading to estrogen dominant symptoms- bloating, fluid accumulation, weight gain, breast tenderness etc.

Lifestyle recommendations: Caffeine can elevate estrogen levels by 80%, so someone with high estrogen levels, or estrogen dominance should avoid caffeine. In addition, people with SNPs in these genes should consider testing for estrogen metabolism to make sure they are metabolizing estrogen to healthy (cancer preventative) vs. unhealthy forms (cancer causing) of estrogen.

CYP2A6, 2C19, 2C92, and 2C93 - These genes are responsible for helping to metabolize a number of drugs, including aspirin and other non-steroidal anti-inflammatories (ibuprofen [Advil, Motrin], naproxen [Aleve]) as well as blood thinners like coumadin, and warfarin. **Lifestyle recommendations:** Individuals with variants in these SNPs will be sensitive to these drugs and should use them with caution.

CYP2D6 – This gene is involved in detoxing pharmaceutical medications from the liver. For example, someone with the T2850C SNP will get extremely sleepy after taking a low dose of Benadryl and be unable to function yet someone without the SNP may feel a little tired with taking the same low dose of Benadryl but be able to function normally. **Lifestyle recommendations:** The Wikipedia.org CYP2D6 page (see attached) lists a number of the drugs that are metabolized by the CYP2D6 genes.

GSTM1, **GSTP, GSTP1 –** These genes are involved in supporting glutathione-s-transferase, which is responsible for healthy levels and function of glutathione. Glutathione is a major antioxidant responsible for reducing oxidative stress in the body. Individuals with SNPs in these genes may have a need for more glutathione to reduce free radicals and decrease oxidative stress. **Lifestyle recommendations:** Eating cruciferous vegetables (kale, cauliflower, broccoli), which contain sulfur, will help the body make more glutathione. **Supplement recommendations:** Glutathione Power

NAT1, NAT2 – These genes are involved in something called acetylation and people who have SNPs in this area may be sensitive to cigarette smoke, carbon fuel emissions, petroleum based products, perfume, leading to a condition called multiple chemical sensitivity.

Acetylation can also cause people to have high or low cholesterol because optimal function of the acetylation pathway is needed to both make and metabolize cholesterol. In addition, they may have low or high acetylcholine levels as the enzyme controlled by this gene acetylates choline to make acetylcholine. Low acetylcholine levels are responsible for the multiple chemical sensitivity symptoms that people with this SNP experience. If acetylcholine levels are low, an individual will have trouble remembering their dreams. If they are high they will have vivid nightmares.

Lifestyle recommendations: The G590A version of this gene is involved in the ability of the liver to metabolize alcohol, so people with a SNP here may not process alcohol well. This G590A gene also metabolizes folate, so red blood cell folate levels may need to be checked if you have this SNP to determine the right amount of folate replacement for you. People with SNPs in this region may find that excessive folate intake does not support their health.

Choline is also required to make phosphatidylcholine, a component of VLDL, which exports fats and cholesterol from the liver. If cholesterol levels are low and/or someone is low in choline, phosphatidylcholine can be given to bring their cholesterol levels up by promoting its healthy release from the liver.

L-carnitine, Alpha Lipoic Acid and CoQ10 may be recommended to break down cholesterol if cholesterol levels are high and multiple SNP's are present in this area.

Supplement recommendations: Phosphatidylcholine, L- carnitine, ALS, CoQ10

SOD2 – This gene makes an antioxidant called superoxide dismutase (SOD) which is responsible for neutralizing oxygen free radicals. It is also necessary for healthy liver function. The SOD enzyme requires manganese to function properly and individuals with this SNP have an increased need for manganese.

Genetically modified foods (soy, corn, canola oil or factory farmed meats, and genetically modified grains) contain something called glyphosate which can chelate or bind up manganese and make it unusable in the body. **Lifestyle recommendations:** People with a SOD2 SNP's should be careful to avoid all GMO foods (soy, corn, canola oil or factory farmed meats, and genetically modified grains).

Manganese deficiency with glyphosate exposure can cause male infertility due to decreased sperm motility. SOD2 SNP's are also related to risk for ALS or Lou Gehrig's disease. If you have multiple yellow or red SNPs in this section it is worthwhile to get manganese levels drawn. Additionally it is worthwhile to get a ferritin level because in the presence of SOD2 SNP's and manganese deficiency the risk of cardiovascular disease increases significantly. See Uniprot.org.

Supplement recommendations: Core Multi, Multivitamin w/antioxidants/EFAs, Complete Mineral Complex

PON1 – This gene is responsible for breaking down of chemicals like the insecticides parathion and DDT. Individuals with this SNP will have an increased risk of coronary artery disease, diabetes and kidney disease. **Lifestyle recommendations:** These people should be faithful in avoiding environments and foods where these chemicals have been sprayed for instance fruit, cotton, wheat, vegetables, and nuts. In addition it is also important for these people to avoid GMOs (soy, corn, canola oil or factory farmed meats, and genetically modified grains).

Tongue Tie and Cleft Palate

CTH S4031I – This gene is involved in converting cystathionine to cysteine. Individuals homozygous (red) for this SNP may be low in cysteine and hence low in glutathione causing an increased risk of having a baby with cleft palate and/or tongue tie. **Lifestyle recommendations:** People with this SNP should eat healthy meats which are high in cysteine. **Supplement recommendations:** N-acetyl cysteine.

Allergy and Mold

HLA – The HLA genes code for proteins that function to create a healthy immune system. Individuals with SNPs in the HLA SNP's (rs7775228, rs2155219) are more susceptible to hay fever, grass pollen, pet dander, dust mite and mold allergies. They are also more prone to inflammation. Those with HLA rs2155219 are at higher risk for developing Crohn's Disease and should watch their secretory IgA (sIgA) levels, a critical building block for a healthy immune system and healthy gastrointestinal tract. sIgA levels should be measured in people with these SNPs. **Lifestyle recommendations:** Eliminate foods that cause gastrointestinal distress. **Supplement recommendations:** Probiotic synergy, PaleoMeal Whey, PaleoFiber.

IgE

People with SNP's here will have mast cell issues leading to hives and rashes due to elevated IgE levels. They should have IgE levels measured.

IgG

The **GSTM3** SNP is important for detoxification and healthy antioxidant function in the body. Antioxidants decrease the free radical load to the body. This section of genes is also important for healthy immune function. **Lifestyle recommendations:** Eat a diet of whole foods full of color. Minimize exposure to toxins from GMO foods, skin care products, plastics, etc. **Supplement recommendations:** Multi w/EFAs and Antioxidants, Antioxidant Defense, Glutathione Power.

IgA

HLA-DQA2 – Individuals with a SNP here are at increased risk for Celiac Disease and deficiency of sIgA which is important for a healthy gastrointestinal tract. **Lifestyle recommendations:** People with SNP's here should have their thyroid antibodies

checked and consider eliminating grain, dairy, and soy from their diet. **Supplement recommendations:** Probiotic synergy, PaleoMeal Whey, PaleoFiber.

Clotting Factors

CETP – This gene is involved in breaking down cholesterol, so individuals may have high cholesterol if they have this SNP even on healthy diets. **Lifestyle recommendations:** Watch cholesterol in foods.

CYP4V2, GP6, ITGB3, KNG – SNPS in these genes all raise the risk of pulmonary embolism, deep vein thrombosis, and stroke and excessive platelet activity. **Supplement recommendations:** Natto serrazimes.

NR1I12, SERP, HRG, F11- these SNP's are all involved with platelet dysfunction leading to increased clotting risk. **Supplement recommendations:** Natto serrazimes.

F10 – This gene may cause low platelet counts causing an increased risk of bleeding.

F7, F2, F5, F9 – People with SNP's in this region can also have excessive platelet function which can put them at risk for a clotting event. Individuals with the SNP's F2 20210A or the F5 Factor V Leiden specifically are at a significantly elevated risk for a clotting event. These people should have their platelet count and platelet function checked.

We don't see people that are homozygous (red) for F2 and F5 because they typically die. It is even rare to see people here who are heterozygous (yellow) for F2 and F5. If people with these SNP's have been on Cipro or Levaquin they may have anti-phospholipid syndrome and elevated fibrinogen because genes in this region are activated by these medications. Fibrinogen levels and function should be checked in these people. **Supplement recommendations**: Natto serrazimes

Methylation

ACE, ADD1, and AGT – These genes are involved in potassium, magnesium and sodium regulation. Individuals with a SNP in either of these genes may be at increased risk for hypertension. The ACE gene can be activated by fluoride, including fluoroquinolones (Ciprofloxin or Levaquin).

Checking **intracellular** sodium, potassium and magnesium levels is important for people with SNP's in these areas. They may have high sodium and low potassium and magnesium- these levels are important to measure if the individual is hypertensive. This could be key in treating them as opposed to putting them on a medication for high blood

pressure. SNP's in the ACE gene can lead to a greater risk of heart attack, stroke or kidney failure. However, this risk can be significantly decreased by healthy living.

ACAT1 – This gene is involved in cholesterol metabolism and breaking down ketones. Individuals with this SNP tend to be adeno-B12 deficient and will do well with the adenosyl-B12 form of B12. Individuals with SNPs in this area are at higher risk for infection by *C. difficile*. People with this SNP should consider using doxycycline and will need a good probiotic. This gene is also related to ulcerative colitis and people with SNP's here can develop ulcerative colitis after antibiotic use.

AHCY – This gene regulates S-adenosyl homocysteine and Sam-e ratios and individuals with this SNP may have chemical sensitivity issues (sensitivity to perfume, cigarette smoke, etc.). There may be a need for Sam-e supplementation in people with this SNP.

BHMT – This gene encodes a cytosolic enzyme that catalyzes the conversion of betaine and homocysteine to dimethylglycine and methionine, respectively. The pathway is involved in making glutathione. It is considered a short cut through the methylation pathway. Individuals may benefit from taking trimethylglycine (betaine) to make glutathione if B12 and folate pathways are not functioning properly and need to be normalized. Beets, lamb, and spinach are good sources of trimethylglycine (betaine).

If after taking TMG you experience panic attacks and anxiety, you need to be checked for COMT and evaluated for elevated epinephrine, norepinephrine, dopamine levels, because methyl groups can increase the levels of these neurotransmitters and lead to these symptoms. People with these SNP's and anxiety may benefit from a phospholipid complex. It is important to look for Lyme Disease, and ask about history of Ciprofloxin or Levaquin use in people experiencing anxiety with phospholipid use, they likely have anti-phospholipid syndrome.

It is important for homocysteine levels not to go below 5 because it puts people at risk for stroke and neuroimmune syndrome.. If homocysteine levels are too low, typically they are low in methionine or they have SNP's in the CBS gene.

Betaine HCl can be given as a digestive aid before meals for people with BHMT SNPs. If they have *H. pylori* be aware that Betaine HCl can give them a very bad upset stomach.

CBS – This gene is involved in the transulfuration pathway and individuals with SNPs here have problems processing sulfur based foods and supplements. These people are often times recommended to completely remove all sulfur from their diet to improve their inability to metabolize sulfur (Yasko protocol). This can cause problems because sulfur

controls blood pressure. In fact, blood pressure medications often times are effective because they are sulfur containing.

Taking all of the sulfur out of one's diet can cause high blood pressure and the complications related to it. It can also deplete glutathione levels because glutathione production is dependent on sulfur as a building block for this molecule.

Depleted glutathione levels put individuals at risk because glutathione is the master antioxidant required to manage free radicals in the body. It is important to try these people on high and low sulfur diets and see how they feel. This will help to determine the effect of sulfur containing foods on their health and well-being.

If they feel worse on a high sulfur diet, they probably have problems with their transulfuration pathway. Clinically, you can check their ammonia and molybdenum levels. If their molybdenum is low and their ammonia is high you know there is a problem with the transulfuration pathway and processing sulfur. If they are not estrogen dominant, you can give them yucca, butyrate or charcoal to break down ammonia and supplement with molybdenum until molybdenum levels go up to break down the sulfur in their body while keeping some sulfur in their diet.

If they have CBS SNP's and ammonia and molybdenum levels are good but they feel better off of sulfur foods for three days, have them avoid them for a few days out of the week to relieve the sulfur burden. If they feel really bad off of sulfur containing foods they should get back on the sulfur containing foods and supplements. People with the CBS 699T SNP's may solely have low homocysteine levels and no problems processing sulfur. People with multiple CBS SNPs may be low in vitamin B6 and need more B6.

Over use of antibiotics can also cut off the transulfuration pathway leading to sulfur sensitivity as well as leading to leaky gut and high oxalate absorption and levels. These oxalates are toxic to us. Healing the gut and using a low oxalate diet can help.

Oxalates can be tested through organic acid testing. In addition, glyphosate, found in GMO foods, can also block the transulfuration/CBS pathway so if ammonia and molybdenum are fine and they are having problems processing sulfur it may be because the GMO's they are consuming have blocked the transulfuration pathway.

COMT – This gene functions to break down the neurotransmitters epinephrine, norepinephrine, and dopamine as well as drugs for hypertension, asthma, and Parkinson's Disease. Individuals with COMT will benefit from adenosyl- or hydroxyl-B12 versus methylcobalamin. Individuals with G in rs6269 many have low dopamine, epinephrine or nor-epinephrine levels and individuals with an A in rs6269 will have high

levels of these neurotransmitters. 61P199P is associated with low dopamine, epinephrine and norepinephrine.

SNPs in H62H and V158M can cause anxiety in individuals with high epinephrine, norepinephrine and dopamine levels especially when given methyl B12 or methyl folate since these neurotransmitters are not being broken down properly. Niacin helps to break down these neurotransmitters and these individuals may have a niacin deficiency and it should be tested.

If you give hydroxy B-12 to someone and they start to feel flu-like or sore, you must evaluate them for cyanide toxicity (from Cyanocobalamin) because the hydroxyl B12 is chelating the cyanide out of their body. Slow down on the administration of hydroxyl B12 in these individuals.

If you give them adeno-B12 and they feel electricity down their arms and legs they are repairing myelin sheaths because adeno-B12 is capable of doing this nerve repair.

COMT Individuals may also have problems with opiate receptors that can be stimulated by the proteins in dairy (casein) or grain (gluten). Stimulation of these receptors can lead to anxiety when eating these foods.

People with COMT are hard to put under and bring out of anesthesia probably because you have to give them so much anesthetic due to their epinephrine, norepinephrine and dopamine levels being so high.

Niacin, NAD, and D-ribose work to manufacture MTHFR

DAO – This gene is involved in breaking down histamine and histamine sensitivity. Individuals with food sensitivities may be low in this enzyme. Some of these people do fine if they take the DAO enzyme with food. However if you have a leaky gut, you may be sensitive to taking this enzyme causing gut distention or abdominal symptoms when taking it.

Even without this SNP, a vitamin E deficiency can cause a deficiency in DAO enzyme levels and function. Individuals with the DAO rs2070586 SNP may have elevated niacin. DAO SNP's can also cause dopamine levels to be elevated.

DHFR – This gene regulates the dihydroflate receptor and is involved in converting folic acid to folate. Individuals with this SNP may have problems with this pathway. This is important since the number one cause of colorectal cancer is un-metabolized folic acid. Metfolin and Quatrefolic are both forms of methyl-folate that can be considered for supplementation here. Quatrefolic crosses the blood brain barrier much more effectively than Metfolin.

FOLR1, 2, and 3 – These genes regulate folate receptors in the brain and individuals with SNPs in these genes may benefit from Quatrefolic which can cross the blood brain barrier. Folic acid can burn out folate receptors in the brain.

FUT2 – Individuals with SNPs in this gene may be low in *bifidobacterium* and *lactobacillus*, which can place them at a higher risk for Crohn's Disease. They may also have poor vitamin B12 absorption. Children with PANDAs (an antibiotic resistant strep infection) may have worsening neurological symptoms when given *bifidobacterium* because the strep strain they have can feed off the *bifidobacterium*.

G6PD – This gene is involved in the production of NADPH. Individuals with a SNP in this gene may have a higher risk of clotting problems and need natural sources of vitamin C to protect red blood cells. They should also avoid beans. Individuals with a SNP in this gene should avoid Ciprofloxin or Levaquin due to an increased risk for developing anti-phospholipid syndrome (an autoimmune hypercoaguable state with positive antibodies).

These people may have anxiety or neurologic events when taking anything phosphatidyl, liposomal, or with soy lecithin. Treatment includes healing the gut and working on mitochondrial function with NADH, CoQ10, and D-ribose. Use *G6PD deficiency.org.*

GAD1 – These genes are involved in breaking down glutamate into GABA. High glutamate is related to MS, schizophrenia, ALS, Parkinson's and addictions like alcoholism and heroin addiction. Individuals should have their neurotransmitters tested and if out of balance, they should be balanced. They should also avoid high glutamate foods (like MSG) and take GABA.

GAMT – Individuals with a SNP in this gene may not be able to metabolize choline properly and they may need to supplement with creatine. These people may have low muscle tone as an additional indicator that they are creatine deficient. SNPs in this gene are also related to fish odor syndrome (smelling like fish).

GIF(TCN3) – This gene is involved in the transport of B12. Individuals with this SNP will potentially test high for B12 levels with this SNP and still may be exhausted and fatigued. Looking at homocysteine or methylmalonic acid levels (they will be high) is a better indicator of someone's B12 status in these individuals.

MAO A – This gene is involved in the breakdown of dopamine, norepinephrine, and serotonin. Individuals with a SNP in this gene will have low serotonin levels and may have depression and sleep issues (can't get from serotonin to melatonin). Those who have leaky gut are at especially high risk for low serotonin if they have this SNP. Foods high in tryptophan like pumpkin seeds, chicken, or turkey can help increase serotonin

levels. Taking 5-HTP, a precursor for serotonin, may help as well. Getting enough sunshine may also help.

MTHFD1 – This gene is involved in choline and folate metabolism. A sign of choline deficiency is low cholesterol. This gene product requires 5-MTHF, niacin, and riboflavin. See Dr. Andrew Rostenberg at beyond mthfr.com for more information.

MTHFR – This gene is responsible for synthesizing methylfolate and individuals with a SNP in this gene can have folate metabolism issues and folate deficiencies. If folic acid levels are measured here instead of RBC folate, they may be elevated because of the inability to convert folic acid to folate.

This can erroneously cause one to think that the folate pathway is functional. This is important because unmetabolized folic acid is the number one cause of colorectal cancer. Folate is also required for a properly functioning immune system. People with this SNP may have low T cell and natural killer cell function and folate deficiency leading to autoimmune issues such as Hashimoto's and severe immune system dysfunction.

Folate deficiency is also associated with autism as well as neural tube defects at birth. Individuals with multiple SNPs in this area may have low dopamine levels and individuals with the A1298C SNP may also be deficient in BH4. For low dopamine BH4/tetra-hydrobiopterin is an important supplement to take. See the VIMEO video by Amy Yasko.

This gene also helps to regulate homocysteine levels because the gene regulates how homocysteine is processed into the methylation cycle. SNPs in this gene increase the risk of heart disease and cancer and can impact the levels of neurotransmitters like serotonin and dopamine. It is important to look at RBC folate, measure T-cells and NK cell function, and dopamine levels, look at status of FOLR SNPs, which code for folate receptors, and the SLC SNP, which is a folate transporter gene. There is a great need for niacin as well as methyl-folate (MTHF) in these individuals. Riboflavin is a cofactor in this pathway.

SNPs at MTHFR A1572G can lead to high homocysteine and blood pressure regulation issues.

MTHFS – This gene is involved in the synthesis of methylfolate and it requires magnesium as a cofactor to function. Individuals with this SNP may have an increased need for magnesium and/or methylfolate.

MTR/MTRR – These genes work together to regenerate and use B12 in the methylation cycle to convert homocysteine to methionine. Individuals with a SNP may have low

homocysteine and need methionine and or SAMe. People with SNP's in these genes may have a greater need for B12. Homocysteine levels should be checked and if low these individuals may need methionine, SAMe, or lithium for B12 transport support. MTRR K350A even if it is heterozygous (yellow) should be addressed because this SNP down regulates B12 and can lead to high homocysteine.

NOS2 and NOS3 – These genes are involved in ammonia detoxification in the urea cycle. Individuals with SNPs in these genes may have elevated ammonia and cholesterol levels. ALA, carnitine, and fish oil should be given cautiously and alternated with these individual while keeping an eye on their ammonia levels.

PEMT – This gene is involved in choline, folate and cholesterol metabolism. Individuals with SNPs in this gene may have an increased need for choline from fats and animal sources of foods such as, eggs, etc., to make cholesterol. They usually also need more folate. People with these SNP's should likely not be vegan. Individuals with low cholesterol will be low in choline and low in folate.

SHMT – This gene shifts the emphasis from the methylation cycle to new DNA synthesis for making cells. Individuals with SNPs in this gene may have high homocysteine and/or drain intermediate products in the methylation cycle. They may also have an increased risk for inflammation in the gut and individuals who experience a bacterial infection may not recover well from infection especially if they additionally have MAO and MTHFR SNPs. These individuals may be low in serotonin and folate and often need folinic acid before taking MTHF. Folinic acid can get the MAO A and MTHFR pathways working again.

SUOX – This gene is responsible for converting sulfite to sulfate and requires molybdenum to function and reduced function can impair brain function. Avoid sulfite containing foods such as wine, dried fruits, processed meats and other foods containing sodium bisulfite or other sulfites. Reduced glutathione and melatonin are recommended to reduce oxidative damage and protect the brain.

TCN1 and TCN2 – This gene is involved in B12 transport and may indicate an increased need for vitamin B12. The best way to check for B12 function is not to measure a B12 level, but rather to measure homocysteine or methyl-malonic acid, which looks at the function of B12 in the body. An elevated B12 level may not mean high or even adequate levels but rather, it may be a sign that the person cannot utilize B12, which leads to a buildup of B12 in the body.

VDR BSM – This gene codes for the vitamin D receptor. Individuals with SNPs here may have an increased need for vitamin D3 and it's important to have levels tested to optimize Vitamin D for these people.

Celiac Disease

HLA DQA1 – This gene encodes an antigen presenting protein that functions in the immune system. Individuals with a SNP in this gene have an increased risk for Celiac Disease and autoimmunity and may need to avoid all gluten-containing foods and supplements.

Thyroid

CTLA4 – This gene codes for a protein that inhibits T cells in the immune system. Individuals with a SNP in this gene are at increased risk for Hashimoto's and gluten intolerance.

FOXE1 – This gene is involved in the formation of thyroid hormone. Individual's with a SNP's in this gene may have a lower ability to convert T4 to T3 and may experience high levels of anxiety.

Eye Health

BCMO1 – The BCMO1 gene is important to eye health and is involved in converting β carotene into vitamin A. Low Vitamin A is associated with poor immune function as well as inability to absorb iodine which is important for thyroid hormone production. Individuals with SNPs in this gene may be low in vitamin A and may benefit from taking cod liver oil which has vitamin A.

Mitochondrial Function

ATP – This gene is involved in cellular energy production in the mitochondria. People with SNPs here will have chronic fatigue, fibromyalgia and poor energy. Levaquin and Ciprofloxin can cause issues in people with these SNPs. Consider giving NADH, CoQ10, d-Ribose, and ATP supplements to build healthy mitochondrial function.

COX5A, and 6C – These genes encode for an enzyme that functions in ATP and energy production in the mitochondria also. People with SNPs here will have chronic fatigue, fibromyalgia and poor energy. Levaquin and Ciprofloxin can cause issues with these SNPs. Consider giving NADH, CoQ10, d-Ribose, ATP supplements to build healthy mitochondrial function.

NDUFS3, 7 and 8 – These genes are involved in the production of energy in the mitochondria in cells. Mutations in NDUFS8 are associated with Leigh Syndrome. People with SNPs here will have chronic fatigue, fibromyalgia and poor energy. Levaquin and Ciprofloxin can cause issues with these SNPs. Consider giving NADH, CoQ10, d-Ribose, ATP supplements for healthy mitochondrial function.

Other Immune Factors

4q27 – In mammals, this gene is thought to function in the regulation of epithelial growth and differentiation, and in tumor development. When the risk allele is GG, it is related to gluten intolerance. When it is TT, it is related to rheumatoid arthritis.

APOE – This gene product is involved in removing VLDL remnants from circulation. Individuals with the APOE4-4 genotype (with a double copy variant in rs429358 (red, +/+) and are CC in rs7412) are at an increased risk for Alzheimer's Disease and will do better on a low fat diet. They should also avoid factory/grain raised animals that have higher levels of omega 6 versus omega 3 and eat only grass fed and free range protein sources high in omega-3's. Sometimes these individuals even need to go vegan to avoid all animal fat. It is wise to measure omega-3 and omega-6 ratios in these people. People that are APOE 4 may do better with unmethylated forms of B12, such as adenosyl B12. ApoE 2/2's people may have issues with carbohydrate intake.

ATG, GSDMB, HLA DRB1, IL5, IL13 – These genes are all markers for inflammation. HLA DRB1 is an inflammation marker for Multiple Sclerosis. The pharmaceutical industry already has H1 and H2 histamine blockers (antihistamines) and is working on IL5 and IL13 blockers. Individuals with SNPs in IL13 that suffer from asthma may not do well on traditional asthma medications (albuterol) and may do well with IL13 blockers.

MeFV – This gene is related to Mediterranean fever and is associated with elevated IgD. Individuals with SNPs in this area suffer from chronic infections/fevers and these people may have Mediterranean fever. They need IgD levels tested. Mediterranean fever is an autoinflammatory disease characterized by fever, pain and amyloidosis. If they have Mediterranean fever, they may do well with Mediterranean fever medications.

STAT4 – SNP's in this gene can cause inflammation and gluten intolerance. These SNPs have been linked to lupus and rheumatoid arthritis. In addition, these SNPs affect the production of T cells which are necessary for a healthy immune system.

TNF-308 – The product of this gene is involved in the regulation of a wide spectrum of biological processes including cell proliferation, differentiation, cell death, lipid metabolism, and coagulation. It has been implicated in a variety of diseases, including

autoimmune diseases, insulin resistance, and cancer and is involved in the inflammatory pathway.

Sulfonotransferase

SULT1A1 and 2A1 – These genes are involved in estrogen metabolism and the metabolism of bile salts made in the galbladder. Individuals with SNPs in these genes may have an increased risk for metabolizing estrogen into procarcinogenic vs. anticarcinogenic forms of estrogen as well as gall bladder issues possibly leading to gallbladder removal surgery.