StrateGene®

Strategic Genetic Analysis

Presented by SeekingHealth®

Prepared For: ascallion

What you're about to uncover in these upcoming pages is extremely powerful!

You finally have the opportunity to 'peek under the hood' and see You.

By discovering your unique genetic makeup using StrateGene®, you'll learn how you can truly optimize your life.

There is no such thing as a "bad" report, or a "good" report—just unique. You won't find any 'red' or 'yellow' colors here that symbolize 'bad' or 'warning'. Instead, you'll learn that some of your genes naturally work slower and some naturally work faster. It's important that you know this information so you can adapt. If you don't know how your genes are built, you've no idea how your choices impact you.

You can change the way your genes function by changing your environment, mindset, food, and lifestyle. Your StrateGene® Report helps you make targeted choice after targeted choice which creates the optimal environment for your genes—one choice at a time. The result? You'll ultimately function at your best—and you'll know why.

Your journey to the best version of You is about to begin!

Here is where you start: 👉 "How to Understand Your StrateGene® Report" 👈

To get the most out of your report, we encourage you to have a health professional help you analyze your StrateGene® Report. They will help you implement specific recommendations. It will be more efficient, cost-saving, and rewarding.

Important Disclaimer:

Although this report may provide useful diagnostic information, StrateGene.Me, Dirty Genes LLC, and Seeking Health LLC do not make or suggest any specific diagnosis or therapeutic course of treatment or action. Any such diagnosis and/or treatment plan is strictly a matter between the patient and their qualified healthcare professional.

To best navigate this report, we highly recommend saving and reading it on Acrobat Reader (For PC users) or Preview (For Mac users).

Raw Data Generation Date: 04-25-24 UTC
Detected Data File Type: AncestryDNA v2

Report Date: 04-25-24 04:05:54 UTC
Report Version: StrateGene® Core v1.1 (44.1)
Report ID: ascallion

Your StrateGene® Genetic Overview

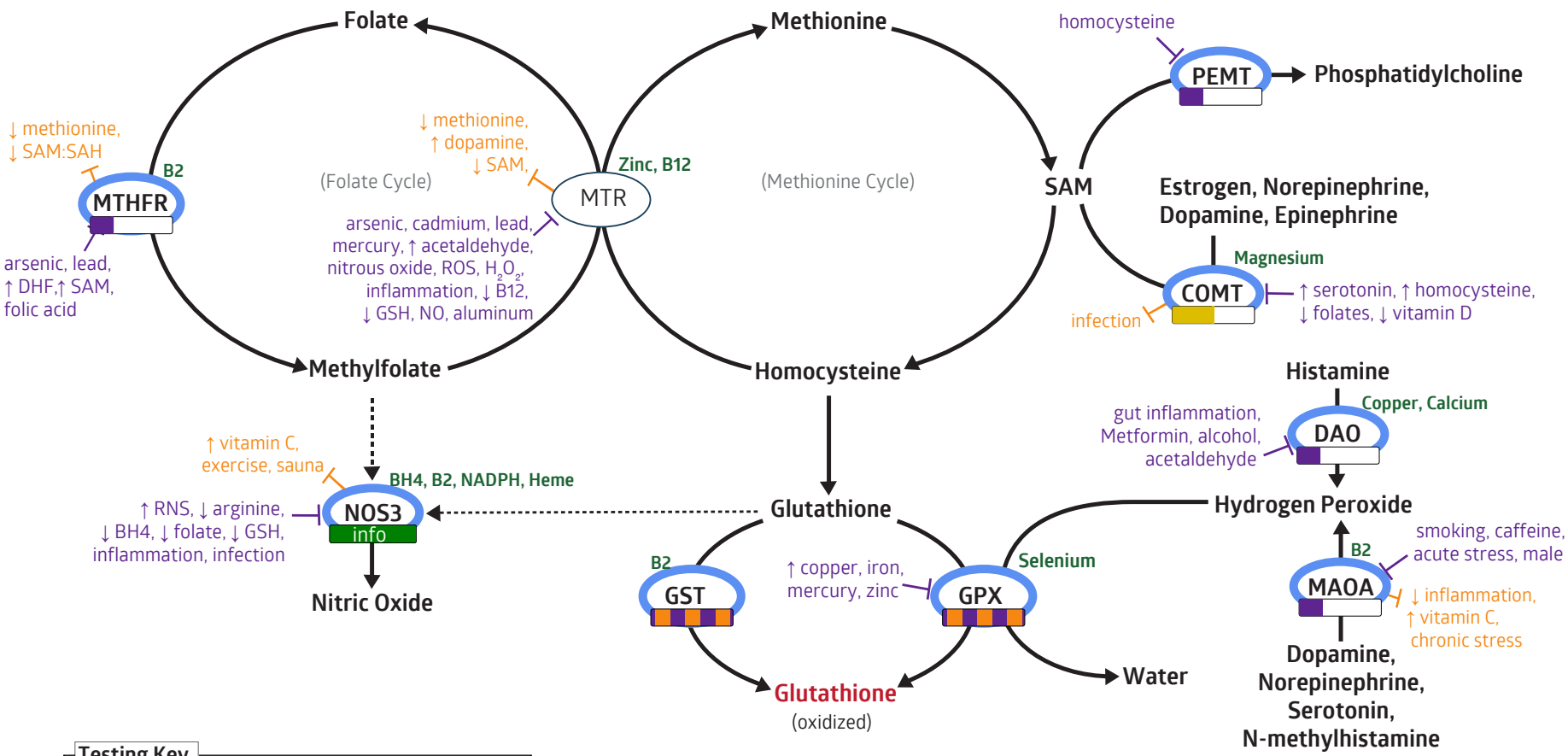
This page is a springboard for finding information that may be the most interesting or relevant for you in this report.

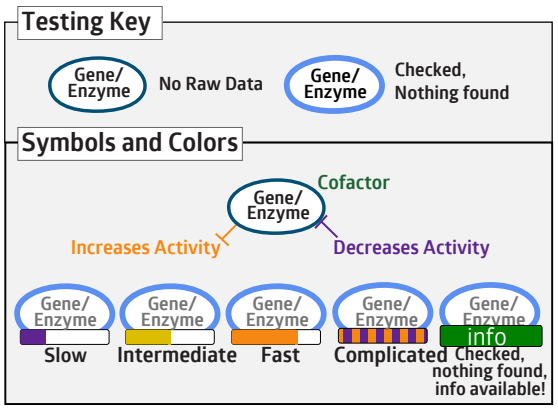
All genes are clickable except the grayed out ones, but you may want to start with focusing on the underlined genes as we found significant and notable variation in them in your data.

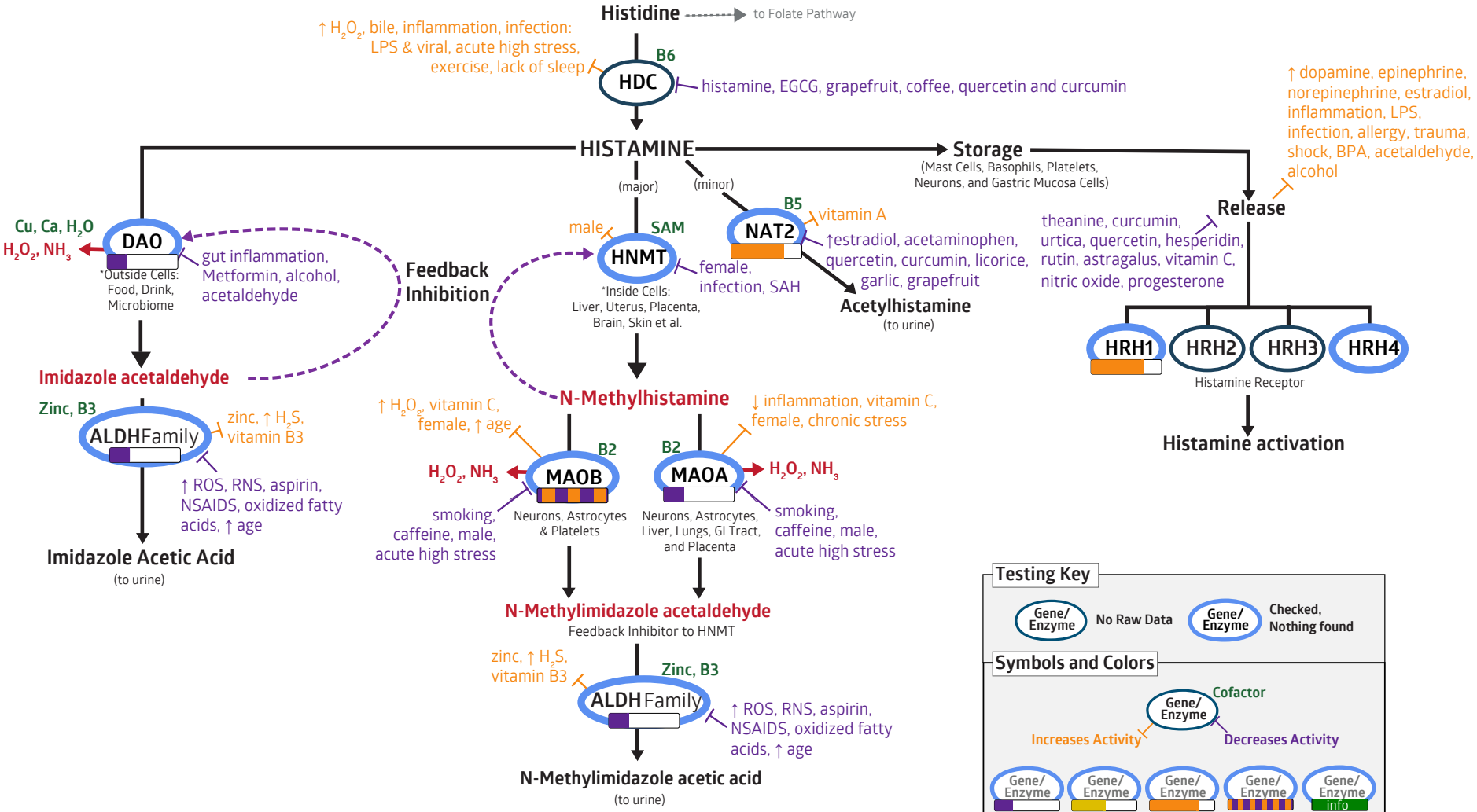
Histamine	Dopamine	Serotonin		Folate	SAM	Glutathione		Biopterin
HRH1	TH	IDO2	ADH1B	SLC19A1	MTR	CBS	NOX/CYBA	GCH1
HRH4	DDC	TPH1	ADH1C	DHFR	MTRR	CTH	SOD2	SPR
DAO	MAOA	TPH2	ALDH2	MTHFD1	TCN1	SUOX	SOD3	NOS3
HNMT	MAOB	DDC	ASMT	MTHFR	TCN2	GCLC/M	GPX1	DHFR
NAT2	DRD2	HTR2A	MTNR1B	FTCD	MAT1A	GSR	GPX4	
MAOA	SLC6A3	HTR2C	CYP1A2	SHMT1	PEMT	G6PD	CAT	
MAOB	DBH	HTR3A	CYP1B1	TYMS	GAMT	GSTA1	MPO	
ALDH1B1	PNMT	HTR3B	SULT1A1		CHDH	GSTO1	GGT1	
ALDH2	COMT	MAOA	UGT1A6		ALDH7A1	GSTO2		
	SLC6A2	MAOB			BHMT	GSTP1		
	ADRB1				DMGDH			
	ADRB2				ADA			
	ADRB3				ADORA2A			
	ALDH2				PON1			
	SLC18A1				PON2			

Key to this table

GENE	Gene is in your data and it was checked
GENE	Gene is not in your data or wasn't checked
GENE	Very important variation found
GENE	Moderately important variation found
GENE	Less important variation found, or general information is available
GENE	No information available


Folate
Methionine
homocysteine
PEMT
Phosphatidylcholine
↓ methionine,
↓ SAM:SAH
B2
MTHFR
arsenic, lead,
↑ DHF,↑ SAM,
folic acid
(Folate Cycle)
↓ methionine,
↑ dopamine,
↓ SAM,
Zinc, B12
MTR
arsenic, cadmium, lead,
mercury, ↑ acetaldehyde,
nitrous oxide, ROS, H_2O_2,
inflammation, ↓ B12,
↓ GSH, NO, aluminum
(Methionine Cycle)
SAM
Estrogen, Norepinephrine,
Dopamine, Epinephrine
Magnesium
COMT
infection
↑ serotonin, ↑ homocysteine,
↓ folates, ↓ vitamin D
Methylfolate
Homocysteine
Histamine
Copper, Calcium
gut inflammation,
Metformin, alcohol,
acetaldehyde
DAO
↑ vitamin C,
exercise, sauna
BH4, B2, NADPH, Heme
↑ RNS, ↓ arginine,
↓ BH4, ↓ folate, ↓ GSH,
inflammation, infection
NOS3
info
Nitric Oxide
Glutathione
Hydrogen Peroxide
smoking, caffeine,
acute stress, male
B2
MAOA
↓ inflammation,
↑ vitamin C,
chronic stress
B2
GST
↑ copper, iron,
mercury, zinc
GPX
Selenium
Water
Glutathione
(oxidized)
Dopamine,
Norepinephrine,
Serotonin,
N-methylhistamine


Testing Key
Gene/ Enzyme
No Raw Data
Gene/ Enzyme
Checked, Nothing found
Symbols and Colors
Cofactor
Gene/ Enzyme
Increases Activity
Decreases Activity
Gene/ Enzyme
Slow
Gene/ Enzyme
Intermediate
Gene/ Enzyme
Fast
Gene/ Enzyme
Complicated
Gene/ Enzyme
info
Checked, nothing found, info available!


Histidine
to Folate Pathway
↑ H2O2, bile, inflammation, infection: LPS & viral, acute high stress, exercise, lack of sleep
B6
HDC
histamine, EGCG, grapefruit, coffee, quercetin and curcumin
HISTAMINE
Storage
(Mast Cells, Basophils, Platelets, Neurons, and Gastric Mucosa Cells)
↑ dopamine, epinephrine, norepinephrine, estradiol, inflammation, LPS, infection, allergy, trauma, shock, BPA, acetaldehyde, alcohol
Release
theanine, curcumin, urtica, quercetin, hesperidin, rutin, astragalus, vitamin C, nitric oxide, progesterone
(major)
(minor)
Cu, Ca, H2O
H2O2, NH3
DAO
*Outside Cells: Food, Drink, Microbiome
gut inflammation, Metformin, alcohol, acetaldehyde
Feedback Inhibition
male
SAM
HNMT
*Inside Cells: Liver, Uterus, Placenta, Brain, Skin et al.
female, infection, SAH
B5
NAT2
vitamin A
↑estradiol, acetaminophen, quercetin, curcumin, licorice, garlic, grapefruit
Acetylhistamine
(to urine)
HRH1
HRH2
HRH3
HRH4
Histamine Receptor
Histamine activation
Imidazole acetaldehyde
Zinc, B3
ALDHFamily
zinc, ↑ H2S, vitamin B3
↑ ROS, RNS, aspirin, NSAIDS, oxidized fatty acids, ↑ age
Imidazole Acetic Acid
(to urine)
N-Methylhistamine
↑ H2O2, vitamin C, female, ↑ age
↓ inflammation, vitamin C, female, chronic stress
B2
MAOB
MAOA
H2O2, NH3
smoking, caffeine, male, acute high stress
Neurons, Astrocytes & Platelets
Neurons, Astrocytes, Liver, Lungs, GI Tract, and Placenta
N-Methylimidazole acetaldehyde
Feedback Inhibitor to HNMT
zinc, ↑ H2S, vitamin B3
Zinc, B3
ALDH Family
↑ ROS, RNS, aspirin, NSAIDS, oxidized fatty acids, ↑ age
N-Methylimidazole acetic acid
(to urine)
Testing Key
Gene/Enzyme
No Raw Data
Checked, Nothing found
Symbols and Colors
Cofactor
Increases Activity
Decreases Activity
Slow
Intermediate
Fast
Complicated
info
Checked, nothing found, info available!

THE HRH1 GENE

The HRH1 (histamine receptor H1) gene expresses a receptor for the ubiquitous messenger molecule histamine.

When histamine engages the HRH1 receptor, it causes smooth muscle contraction, increase in capillary permeability, release of catecholamines from the adrenal gland, and neurotransmission in the central nervous system.

HRH1 has been associated with multiple processes, including memory and learning, sleep and circadian rhythm, and thermoregulation.

Dirties your HRH1 gene

Supplements and Medications: Many medications interact with this enzyme, consult your healthcare provider or pharmacist.

Cleans your HRH1 gene

Supplements and Medications: Antihistamines (Benadryl), hesperidin

Notable variation:

SNP: **HRH1 -17T>C rs901865 (+/-, TC)**

No functional studies exist for this TC variant, but it is thought to be a true functional variant affecting receptor density in an adverse way that may increase allergy risk. Clinical observation suggests TC carriers may be at increased risk for motion sickness and electromagnetic sensitivity.

THE DAO (AOC1) GENE

The DAO (diamine oxidase or amine oxidase aka AOC1) gene expresses an enzyme which catalyzes the degradation of compounds such as histamine and polyamines (putrescine, spermine, and spermidine) to form hydrogen peroxide (H_2O_2) and ammonia (NH_3). Copper (Cu) and calcium (Ca) are cofactors for this reaction.

Histamines are involved in allergic and immune responses, gut motility and gastric acid secretion, inflammation, acts as a neurotransmitter, etc, etc.

Polyamines are involved in cell proliferation, tissue differentiation, tumor formation, and possibly pre-programmed cell death (apoptosis).

Histamine and polyamines metabolized by DAO come from foods, drinks and bacteria found in the digestive tract.

Placental DAO is thought to play a role in healthy pregnancy as high histamine during pregnancy leads to many pregnancy complications. Thus, DAO is a very important gene to keep clean during pregnancy. DAO is feedback inhibited by its end product so be sure the ALDH family of genes is functioning well.

Important Notes:

- The more the DAO enzyme reduces histamine, the more hydrogen peroxide and ammonia are produced. These compounds are quite reactive and may damage the intestinal lining and contribute to numerous problems.
- As with many genes, DAO is heavily influenced by the environment, food and lifestyle. Even if one does not have variants, the DAO gene may be significantly underperforming leading to histamine intolerance.
- Histamine intolerance is extremely common and really impacts one's quality of life. Be sure to read the DAO chapter in *Dirty Genes* and take the quiz to see how your DAO is acting in real time.

Notable variation:

SNP: **DAO (AOC1) -691G>T rs2052129 (+/+, TT)**
This TT variant exhibits 20% less activity in vitro. This may lead to higher levels of histamine in the intestinal tract and possible increase in systemic histamine.

SNP: **DAO (AOC1) 47C>T rs10156191 (+/+, TT)**
This TT variant exhibited approximately 30% less activity compared to wild type. This may lead to higher levels of histamine in the intestinal tract and possible increase in systemic histamine.

An AOC1 Slow Haplotype
Having one or more minor alleles in at least 2 of the 3 rsid#s appears to reduce DAO activity compared to having a single variant. Thus, the variants appear to be additive in their ability to decrease DAO activity. Individuals HOM for the minor allele in all three SNPs (6 risk alleles) exhibit 90% less mRNA (and presumably similar reduction in activity) compared to individuals HOM wild type (0 risk alleles). Those with 1-5 alleles fall somewhere along that gradient. One study observed almost 1 in 5 people with low DAO mRNA had no symptoms suggesting other genetic and environmental factors are at play.

Gene	rsID	Alias	Variant Allele	Call
DAO (AOC1)	rs10156191	47C>T	T	TT
DAO (AOC1)	rs1049793	His645Asp	G	NA
DAO (AOC1)	rs2052129	-691G>T	T	TT

Dirties your DAO (AOC1) gene

Environment: Avoid aldehydes from the environment such as smog, vehicle emissions, smoking (especially secondhand exposures), cooking fumes, formaldehyde from building materials; xenoestrogens. The harder the DAO enzyme need to work in order to detoxify these environmental chemicals, the more ammonia (NH_3) and hydrogen peroxide (H_2O_2) are produced as by-products.

Lifestyle: Avoid alcohol, especially red wine and champagne. Alcohol is especially problematic if individuals have inherited either a fast ADH1B (not present) and/or fast ADH1C (not present) and/or slow ALDH2 (present) and/or slow ALDH1B1 (present). Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections. Some gastrointestinal tract bacteria are big producers and/or stimulators of histamine as well as the common parasite: *Blastocystis hominis*.

Food: Avoid known food allergies and intolerances, leftovers, histamine liberating foods, non-fresh foods especially fish and meat.

Indirectly, high protein meals may increase histamine as well via increased histidine substrate. Histidine is an amino acid found in protein. Histidine is the substrate for the HDC gene which makes histamine. By consuming excessive protein, one may also increase histamine.

Supplements and Medications:

- Be very mindful of what probiotics you are taking. *Lactobacillus fermentum* and *L. bulgaricus* are known to increase histamine.
- If side effects from the DAO enzyme supplement occur, it may be due to the increased ammonia and hydrogen peroxide produced as reactive metabolites. Consult your healthcare provider or pharmacist.
- Many medications interact with this enzyme. Metformin, Tagamet, Verapamil and Amiloride are known to slow DAO.

Cleans your DAO (AOC1) gene

Environment: When traveling in high risk countries, use a quality water filter which removes bacteria and parasites such as *Blastocystis hominis*.

Lifestyle: Healthy digestion with good levels of pancreatic enzymes, bile and stomach hydrochloric acid. Pregnancy increases DAO enzyme as the placenta produces DAO. This is a big reason why some women feel better during pregnancy.

Cleans your DAO (AOC1) gene, continued...

Food:

- Focus on B6, calcium and copper rich foods, and identify lower histamine containing foods and choose them as staples. Typically, the more aged a food or drink is, the more histamine it contains.
- Rinsing meat and meat prior to cooking is not recommended by food safety guidelines and may spread bacteria in the kitchen. However, carefully doing so may wash off histamine produced by bacteria.
- Rinsing lunch deli meats and patting dry prior to assembling sandwich or eating may support reduction in histamine.
- Frying and grilling increases histamine level in meat while stewing/braising/boiling has little influence or even decreases it. These methods may help those histamine-sensitive as compared with frying and grilling.
- Optimize protein intake. General recommendation for total protein for the day is 0.8 grams of protein per 2.2 lbs of body weight. Watch the 'Food' video in the Dirty Genes Course to learn more about protein intake.

Supplements and Medications:

- Consider vitamin B6, calcium, copper, additionally consider *Saccharomyces boulardii* especially after a course of antibiotics. Use probiotics which are known to reduce or balance histamine.
- For additional real-time support while drinking or consuming high-histamine foods, use a DAO enzyme supplement. Support elimination of hydrogen peroxide and ammonia by using pyrroloquinoline quinone (PQQ), acetyl-L-carnitine, ornithine, S-acetyl glutathione or liposomal glutathione.
- Also support the ALDH2 enzyme with zinc, vitamin B1 and B3 to break down the acetaldehyde generated by the DAO enzyme.
- If presence of small intestinal bacterial overgrowth (SIBO), consider gallbladder support and/or ox bile. SIBO may increase histamine levels and overtax DAO.
- If DAO is overwhelmed, histamine may be absorbed into the blood and start impacting intracellular histamine levels thereby putting a burden on HNMT. Thus, supporting the HNMT enzyme may be needed in addition to DAO, MAOA, NAT2 and ALDH2. If the HNMT gene is experiencing a heavy workload, then other methyltransferase genes such as COMT, GAMT and PEMT may become slowed.

THE MAOA GENE

The MAOA (monoamine oxidase A) gene produces an enzyme that processes both internally-produced and externally-derived dietary and environmental amines. Riboflavin (B2) is the cofactor and the by-products of this reaction are hydrogen peroxide (H_2O_2) and ammonia (NH_3).

The amount of hydrogen peroxide generated by MAOA is so significant that it consumes large amounts of glutathione.

In the Histamine Pathway, MAO enzymes detoxify histamine. Histamine is a vasoactive amine that acts on blood vessels to alter their permeability and causes vasodilation. Therefore, in addition to their role in maintaining normal mood and brain function, MAO enzymes also play a major role in regulating blood pressure. A side effect of MAO inhibiting medications is orthostatic hypotension (a lightheaded feeling when standing quickly). But combining a MAO inhibiting medication with high tyramine foods can cause high blood pressure.

If MAO enzymes are not functioning well, N-methylhistamine may accumulate. N-methylhistamine causes feed-back inhibition of HNMT, resulting in a build-up of histamine.

This perspective on the Histamine Pathway debunks the popular idea of 'Over and Undermethylation'.

'Undermethylation' is the idea that histamine levels are high due to poor methylation status and low SAM, whereas 'overmethylation' is the idea that histamine levels are too low due to excessive methylation and high SAM.

Indeed, HNMT requires SAM as a methyl donor in order to process histamine. However, you can have a situation where methylation status is absolutely fine, but histamine levels are still high.

In this case, the cause of high histamine could well be sluggish MAO enzymes and/or sluggish ALDH enzymes and have nothing to do with methylation status.

It has been observed that schizophrenic patients have 2.6 fold higher N-methylhistamine levels in cerebrospinal fluid. This suggests either a fast HNMT or a slow MAOA and/or slow MAOB.

Interestingly, excessive serotonin and high histamine in the brain are associated with migraines. Riboflavin (B2), the cofactor of MAOA, is known to be effective in reducing incidence of migraines and headaches.

MAO enzymes are located on the X chromosome. Therefore, males only inherit one allele and females have inherently higher activity as a result of having two X chromosomes. MAOA activity tends to naturally increase throughout adolescence into adulthood.

Notable variation:

SNP: **MAOA T941G rs6323 (-/-, TT)**

This wild type (TT in women, T in men) appears to possess lower MAOA activity compared to the GG variant. This may slow the clearing out of N-methylhistamine and potentially lead to higher histamine levels.

Slows down your MAOA gene

Environment:

- Research shows a noisy sleep environment (near highway, train tracks, airports, city life, college dorms) increases catecholamine levels and workload on the MAOA enzyme.
- Early childhood mistreatment and maternal stress in utero have been shown to downregulate MAOA.
- Passive exposure to smoke (even in utero) slows the MAO genes. Smoking while pregnant is associated with aggressive traits in offspring.

Lifestyle:

- Short-term, high stress situations reduce the activity of MAO enzymes presumably in order to respond to the "fight or flight" situation by reducing the break down of stress hormones.
- Smoking (strongly) and caffeine (weakly) reduce MAO activity and raise catecholamine levels. Hence people suffering from depression often self-medicate with these substances. Using food and herbs to slow MAO (see below) may help when quitting smoking. Alcohol actually increases MAO activity but some alcohols, at the time of consumption, can overwhelm MAO capacity.
- Alcohols, such as champagne and wine which contain high levels of amines such as tyramine and histamines increase MAO workload and may exacerbate histamine symptoms. MAOA activity may be regulated naturally with healthy foods and supplements (see below).
- Iron deficiency anemia can cause a decrease in MAO activity as research indicates that insufficient levels of dietary iron in the womb can lead to poorer cognitive functioning and maladaptive social behaviors including aggressive temperament in offspring.

Food:

- Riboflavin (B2)-deficient or iron-deficient diet causes cofactor-related enzyme limitations.
- Avoid simple, processed carbohydrates as well as excessive consumption of tryptophan rich foods.
- Foods containing naturally-occurring amines may reduce the capacity of MAO enzymes to detoxify histamine (an internally-produced amine). These include tyramine containing foods: aged cheeses; cured, smoked or processed meat or fish; fermented foods and sauces: yeast spreads (marmite), tempeh, miso, tamari; beer, wine and champagne; tofu and soy milk, fava beans and snow peas.

Slows down your MAOA gene, continued...

Supplements and Medications:

- Excessive tryptophan will dirty MAOA by increasing its workload and this may result in hyperactivity and sweating. Therefore, do not over supplement but use the pulse method instead.
- For those with a fast MAOA genotype that is expressing itself (or your MAOA is acting fast due to other factors such as chronic stress or low estrogen), then these supplements may be useful to calm a fast MAOA: 5-hydroxytryptophan (5-HTP), garlic extract, berberine, curcumin, quercetin, green tea, *Rhodiola rosea*. Many medications interact with this enzyme, especially reversible MAO inhibitors such as pseudoephedrine, ephedrine, norephedrine.
- Beware concurrent use of multiple medications as MAO inhibition effects are often additive. Consult your healthcare provider or pharmacist.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Speeds up your MAOA gene

Lifestyle:

- Chronic, low-level stress causes MAO enzymes to upregulate presumably as a result of the need to break down the increased amount of stress hormones being produced.
- Low estrogen tends to raise MAOA activity. Therefore, the postpartum estrogen drop, as well as perimenopausal estrogen decline, seem to relate to upregulated MAOA levels in the brain. Fluctuations in estrogen during the menstrual cycle may contribute to mood swings through a similar relationship.
- Alcohol increases MAO activity, which may cause a build-up of toxic acetaldehydes if you have fast ADH1B (not present) or slow ALDH1B1 (present) or slow ALDH2 (present). While drinking alcohol is not encouraged, if occasional alcoholic beverages are consumed then low-histamine beverages such as gin, vodka, rum or bourbon are better choices, especially if you take a MAO inhibitor.

Food: Iron, riboflavin (B2), vitamin C and E rich foods along with cruciferous vegetables, eggs or broccoli sprouts support glutathione production and thus supports MAOA indirectly.

Supplements and Medications: Optimize riboflavin (B2) and iron. Vitamin C and vitamin E are free radical scavengers and reduce the hydrogen peroxide produced by MAO. PQQ (pyrroloquinoline quinone), liposomal glutathione or S-acetyl glutathione also support elimination of hydrogen peroxide.

THE MAOB GENE

The MAOB (monoamine oxidase B) gene produces an enzyme that catalyzes the removal of an amine group from both internally-produced and externally-derived dietary and environmental amines. MAOB is the predominant form of MAO in the brain. Riboflavin (B2) is the cofactor and the by-products of this reaction are hydrogen peroxide (H_2O_2) and ammonia (NH_3). The amount of hydrogen peroxide generated by MAOA is so significant that it consumes large amounts of glutathione. MAO enzymes are located on the X chromosome. Therefore, males only inherit one allele and females have inherently higher activity as a result of having two X chromosomes.

In the Histamine Pathway, MAO enzymes detoxify histamine. Histamine is a vasoactive amine that acts on blood vessels to alter their permeability and causes vasodilation. Therefore, in addition to their role in maintaining normal mood and brain function, MAO enzymes also play a major role in regulating blood pressure. A side effect of MAO inhibiting medications is orthostatic hypotension (a lightheaded feeling when standing quickly). But combining a MAO inhibiting medication with high tyramine foods can cause high blood pressure.

If MAO enzymes are not functioning well, N-methylhistamine may accumulate which causes a build-up of histamine due to feed-back inhibition of HNMT.

This perspective on the Histamine Pathway debunks the popular idea of 'Over and Undermethylation'.

'Undermethylation' is the idea that histamine levels are high due to poor methylation status and low SAM, whereas 'overmethylation' is the idea that histamine levels are too low due to excessive methylation and high SAM.

Indeed, HNMT requires SAM as a methyl donor in order to process histamine. However, you can have a situation where methylation status is absolutely fine, but histamine levels are still high.

In this case, the cause of high histamine could well be sluggish MAO enzymes and/or sluggish ALDH enzymes and have nothing to do with methylation status.

It has been observed that schizophrenic patients have 2.6 fold higher N-methylhistamine levels in cerebrospinal fluid. This suggests either a fast HNMT or a slow MAOA and/or slow MAOB.

Interestingly, excessive serotonin and high histamine in the brain are associated with migraines. Riboflavin (B2), the cofactor of MAOB, is known to be effective in reducing incidence of migraines and headaches.

It is also important for the down-stream ALDH enzymes to be working well for the whole pathway to run smoothly.

Notable variation:

SNP: **MAOB -36A>G rs1799836 (-/-, TT)**
Carriers of the T allele have been shown to have average N-methylhistamine levels in cerebrospinal fluid. This suggests wild type activity.

SNP: **MAOB 15106T>C rs5905512 (+/+, AA)**
This variant (AA women, A men) is not yet well studied in terms of its functional consequences. Metabolomic research indicates this mutation may be of importance in men. It is included here for investigational purposes in anticipation of future research that can better characterize its impact.

Slows down your MAOB gene

Lifestyle:

- Limit alcohol (more than one glass), caffeine (weakly inhibits), iron deficiency anemia, smoking (both active and passive exposures) which all inhibit.
- Short-term, acute, high stress situations reduce the activity of MAOB enzymes (as response to the "fight or flight" situation by reducing the break down of stress hormones).
- Males have only one copy, so inherently possess less activity. Stress sensitive females (higher basal heart rate, lower peak estrogen and progesterone) appear to have less activity.

Food:

- Avoid simple, processed carbohydrates; riboflavin (B2)-deficient diet, iron-deficient diet.
- Foods containing naturally-occurring amines may reduce the capacity of MAO enzymes to degrade serotonin (an internally-produced amine). These include tyramine containing foods: aged cheeses; cured, smoked or processed meat or fish; fermented foods and sauces: yeast spreads (marmite), tempeh, miso, tamari; beer, wine and champagne; tofu and soy milk, fava beans and snow peas.
- Avoid excessive consumption of tryptophan rich foods for the same reason.

Supplements and Medications:

- Excessive tryptophan will slow MAOB by increasing its workload and this may result in hyperactivity and sweating. Therefore, do not over supplement but use the pulse method instead.
- For those with a fast MAOB genotype that is expressing itself (or your MAOB is acting fast due to other factors such as chronic stress or low estrogen), then these supplements may be useful to calm a fast MAOB: Garlic extract, berberine, curcumin, quercetin, green tea, EGCG from green tea, silymarin, *Glycyrrhiza spp.* (licorice), *Lamiaceae* (mint family: lavender, oregano, rosemary, sage, thyme, etc); *Rhodiola rosea*, *Scutellaria spp.* (skullcap), *Piper methysticum* (kava-kava), *Baptisia officinalis* (wild indigo), gentian, *Symphytum spp.* (comfrey), *Phellodendron amurense* (Amur corktree), *Cyamopsis psoralioides* (bakuchi seed), *Psoralea corylifolia* (babchi seed).
- Many medications interact with this enzyme, especially reversible MAO inhibitors such as pseudoephedrine, ephedrine, norephedrine. Beware concurrent use of multiple medications as MAO inhibition effects are often additive. Consult your healthcare provider or pharmacist.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bio-identical estrogen (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, or if there are other indications for its use.

Speeds up your MAOB gene

Lifestyle:

- Long-term, low-level ongoing stress causes MAOB upregulation. MAOB activity also naturally increases with age.
- Estrogen tends to inhibit MAOB, therefore an age-related decline in estrogen is likely to further increase MAOB activity.
- Increased MAOB activity will cause an increased throughput of N-Methylimidazole acetaldehyde. It is therefore important that your aldehyde dehydrogenase enzymes (ALDH family) are working well to safely process this out of the body. Those with a slow ALDH1B1 (present) or ALDH2 (present) may be at a disadvantage.
- Not only may high levels of acetaldehydes cause flushing, irritation to the respiratory tract and neuro-inflammation, but N-Methylimidazole Acetaldehyde itself causes feedback inhibition of the HNMT gene (which is the first step in the detoxification of histamine). Therefore, histamine symptoms are likely to increase if MAOB is upregulated and ALDH enzymes are not supported.
- Alcohol also increases MAOB activity. While drinking alcohol is not encouraged, if occasional alcoholic beverages are consumed then avoiding high-histamine ones such as wine and champagne would be advisable. Low-histamine alcohols such as gin, vodka, rum or bourbon are better choices, especially if you take a MAO inhibitor.

Food: Consider riboflavin (B2), vitamin C and E rich along with cruciferous vegetables, eggs or broccoli sprouts to support glutathione.

Supplements and Medications: Optimize riboflavin (B2). Vitamin C and vitamin E, liposomal glutathione, S-acetyl glutathione, PQQ (pyrroloquinoline quinone) and carnosine are free radical scavengers and reduce the hydrogen peroxide produced by MAO.

THE ALDH1B1 GENE

The ALDH1B1 (aldehyde dehydrogenase family member 1B1) gene expresses an enzyme which oxidizes aldehydes. ALDH1B1 is located in the mitochondria and requires NAD+ derived from niacin (B3) as a cofactor.

Dirties your ALDH1B1 gene

Environment: Avoid aldehydes from the environment such as smog, vehicle emissions, smoking (especially secondhand exposures), cooking fumes, formaldehyde from building materials, disinfectants, drugs and perfumes.

Lifestyle: Avoid alcohol and smoking. Work with your healthcare provider to identify and treat intestinal candidiasis.

Food: Avoid known allergens; foods containing acetaldehyde (fermented foods, very ripe fruit, artificial flavors like lemon flavoring, ground and instant coffee).

Cleans your ALDH1B1 gene

Environment: Utilize air filtration systems to remove exposures from airborne aldehydes.

Food: Niacin (B3) rich

Supplements and Medications: Consider niacin (B3). Thiamine (B1) is depleted by aldehydes so adding may support potential deficiencies.

Notable variation:

SNP: **ALDH1B1 ALDH1B1*2 rs2228093 (+/-, TC)**

This CT variant of ALDH1B1 may disrupt cofactor binding due to changes in structural flexibility of the enzyme thus reducing activity as predicted by bioinformatic techniques. Two different cohorts of European ancestry confirmed this predicted effect by slightly increased sensitivity to alcohol.

Note: Due to lack of research in other ethnicities, this observation may be applicable only to those of European descent.

THE ALDH2 GENE

The ALDH2 (aldehyde dehydrogenase family member 2) gene expresses an enzyme which converts aldehydes to carboxylic acids, usually for use in the muscle and heart.

In the Histamine Pathway, ALDH2 helps detoxify acetaldehyde intermediates of histamine using the cofactor niacin (B3).

ALDH2 is best known for its role as the second enzyme in the major pathway for processing acetaldehyde from alcohol. In most people, this acetaldehyde is rapidly transformed to less harmful acetate and water by ALDH2. If acetaldehyde isn't broken down quickly, it accumulates in the liver and body and contributes to a hungover feeling and results in what is known as the "Asian flush".

If the toxic acetaldehydes are not processed quickly enough by the ALDH2 enzyme, then the HNMT and DAO enzymes are instructed to slow down via the mechanism of feedback inhibition. Thus, the high histamine symptoms one is experiencing may not be due to a slow HNMT (not present) and/or slow AOC1 (present). Rather, the histamine symptoms are actually triggered by the dirty downstream effect of the slowed ALDH genes.

Clean up the ALDH genes so the acetaldehydes clear out thereby removing the feedback inhibition on DAO and HNMT. Adequate thiamine (B1) is particularly important in this process. Another possible scenario is fast HNMT and/or DAO that produce excessive acetaldehydes that feedback inhibit these same enzymes. This goes to show that the entire pathway must be supported versus just one gene.

Dirties your ALDH2 gene

Environment: Minimize exposure to aldehydes from the environment such as vehicle emissions, smoking (especially secondhand exposures), cooking fumes, formaldehyde from building materials, disinfectants, drugs, perfumes, fungicides and pesticides, carbon tetrachloride (dry cleaning), hydrogen sulfide and many other environmental chemicals. Minimize oxidative stress to decrease aldehydes created internally by reactive oxygen species.

Lifestyle: Avoid alcohol, smoking, insulin resistance, oxidized LDL, high kynurenine. Work with your healthcare provider to identify *Candida* dysbiosis which generates endogenous acetaldehyde.

Notable variation:

SNP: **ALDH2 699T>C rs737280 (+/+, CC)**

This CC variant may decrease enzyme activity and makes exposures to pesticides more risky. Due to lack of research in other ethnicities, these results may be applicable only to those of European descent.

Dirties your ALDH2 gene, continued...

Food:

- Limit oxidized omega-6 fatty acids (from old or processed oils, microwaved fatty foods).
- Avoid known allergens.
- Avoid foods high in acetaldehyde such as fish products, canned vegetables, fermented foods: yogurt, vinegar, kombucha, fermented mushrooms, tempeh, miso, pickled vegetables and kimchi. Other foods containing acetaldehyde include very ripe fruit, artificial flavors like lemon flavoring, ground and instant coffee. Many aldehydes are found in drinking water so use a filter.
- Avoid foods and drinks containing aspartame which are metabolized to formaldehyde.

Supplements and Medications: Acetaminophen (Tylenol), aspirin and *Pueraria lobata* (kudzu) have been shown to inhibit ALDH2 and worsen symptoms after drinking alcohol.

Cleans your ALDH2 gene

Environment: Employ strategies to reduce exposure to sources of acetaldehyde and other environmental chemicals.

Lifestyle: Filter drinking water

Food: Vitamins C, B1 & B3, zinc, magnesium and resveratrol rich (especially when consuming alcohol), diet rich in vegetables from the brassica family, broccoli sprouts

Supplements and Medications:

- Zinc, niacin (B3), glutathione, sulforaphane, resveratrol with vitamin C (especially when consuming alcohol).
- Thiamine (B1) is especially important as acetaldehyde damages enzymes which are B1 dependent.
- Some herbs have been shown in mice to speed up the biotransformation of acetaldehyde into less toxic end products. These herbs include *Lycium chinense* (goji berry), *Acanthopanax sessiliflorus, Ixeris dentata, Polypori umbellati* (zhu ling).

THE NAT2 GENE

The NAT2 (N-acetyltransferase 2) gene expresses an enzyme which conducts phase II acetylation reactions in the liver which combine the starting product with acetyl-CoA to make the end product less toxic. Pantothenic acid (B5) is a cofactor for this reaction.

NAT2 participates in the acetylation and detoxification of histamine as well as a plethora of hydrazine and arylamine drugs and also carcinogens such as heterocyclic amines.

NAT2 is the minor route of histamine elimination while the HNMT gene processes the bulk of intracellular histamine.

Polymorphisms in the NAT2 gene result in individuals being categorized as rapid, intermediate, or slow acetylators.

Dirties your NAT2 gene

Environment:

- Avoid exposure to environmental arylamine chemicals such as found in the leather, rubber, printing, and textiles industries or to large quantities of paint.
- Avoid diisocyanate, which is in chemicals used in the production of polyurethane products, such as rigid and flexible foams, coatings, adhesives, sealants and elastomers. Workers exposed to these were more susceptible to asthma, especially those with slow NAT2 activity.

Food: Grapefruit is an known inhibitor so best to avoid for slow types especially during times of environmental exposures.

Supplements and Medications: Sadly, there is no research looking at fast/slow acetylators and how they respond to known in vitro NAT2 inhibitors or promoters in real life. Many of these compounds (curcumin, quercetin, garlic) are healthy foods with constituents known to promote health (flavonoids, polyphenols). Therefore do not avoid these, but consider pulsing them, as in not using as daily staples. Acetaminophen may also be problematic for slow types.

Cleans your NAT2 gene

Food: Vitamin A, B5 rich

Supplements and Medications: Consider Vitamin A, B5.

Notable variation:

A NAT2 Fast Haplotype

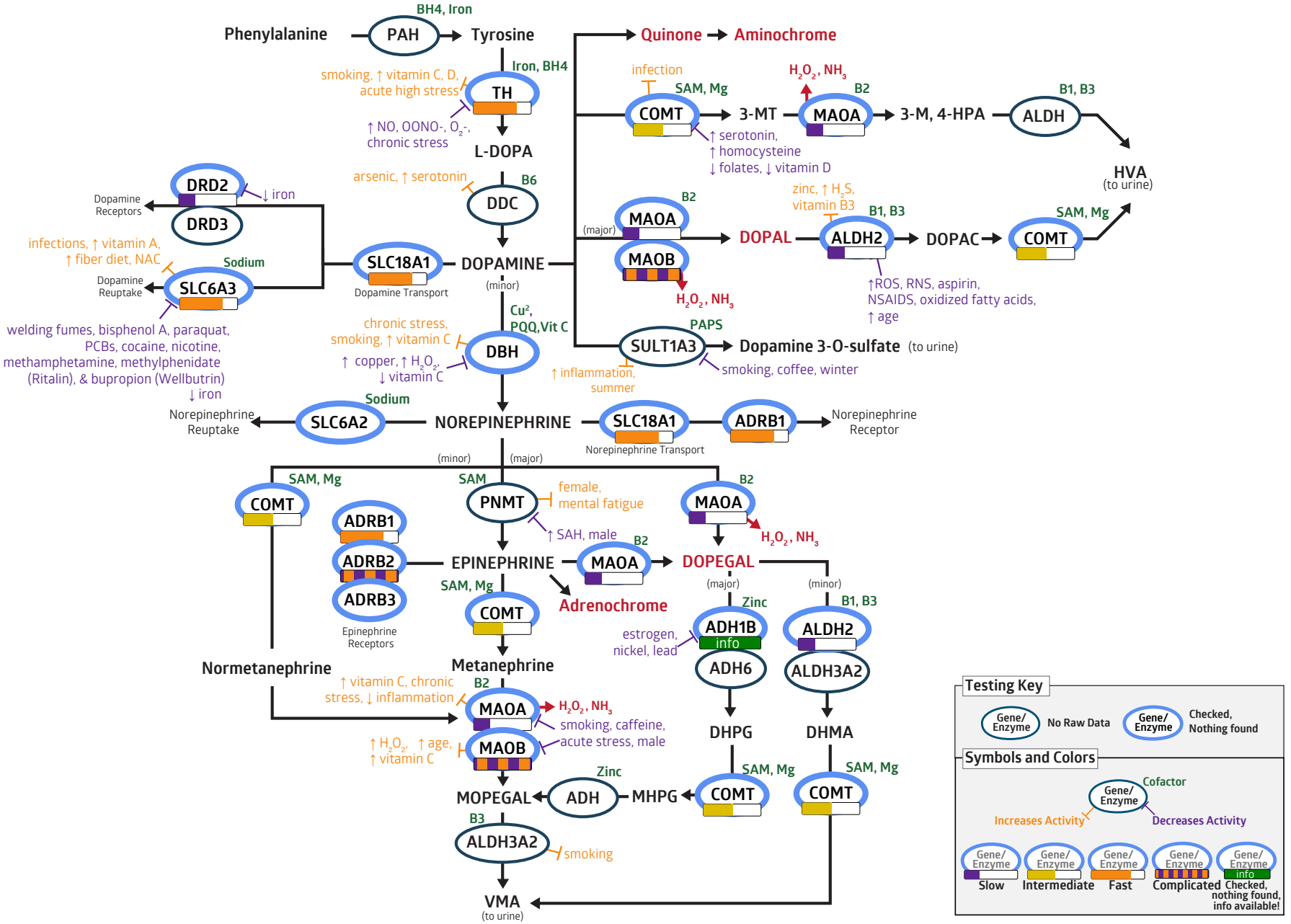
This genotype implies a fast rate of clearance of various drugs, environmental chemicals, and histamine relative to the intermediate and slow genotypes.

Note: This predicted speed is applicable to those of Caucasian ancestry. If you are of another ancestry these results may not be relevant.

Recent research into NAT2 fast versus slow resulted in the opposite speed predicted in persons of same ethnicity and genotype living in vastly different geographic areas. It is presumed that local environmental, dietary and microbiome population differences underlie this observation.

In other words, your genotype (as shown, for example, in this report) may predict one type, but your local environment and lifestyle may influence its expression in the opposite direction.

Gene	rsID	Alias	Variant Allele	Call
NAT2	rs1041983	C282T	T	CC
NAT2	rs1801280	T341C (I114T)	C	TT
NAT2	rs1799929	C481T	T	CC
NAT2	rs1799930	G590A (R197Q)	A	GG
NAT2	rs1208	A803G (K268R)	G	AA
NAT2	rs1799931	G857A (G286E)	A	GG


Phenylalanine
PAH
BH4, Iron
Tyrosine
Iron, BH4
TH
smoking, ↑ vitamin C, D, acute high stress
↑ NO, OONO-, O2-, chronic stress
L-DOPA
B6
DDC
arsenic, ↑ serotonin
DOPAMINE
(minor)
Quinone
Aminochrome
infection
SAM, Mg
COMT
3-MT
H2O2, NH3
B2
MAOA
3-M, 4-HPA
B1, B3
ALDH
HVA
(to urine)
↑ serotonin, ↑ homocysteine, ↓ folates, ↓ vitamin D
DRD2
DRD3
Dopamine Receptors
↓ iron
infections, ↑ vitamin A, ↑ fiber diet, NAC
Sodium
SLC6A3
Dopamine Reuptake
welding fumes, bisphenol A, paraquat, PCBs, cocaine, nicotine, methamphetamine, methylphenidate (Ritalin), & bupropion (Wellbutrin)
↓ iron
SLC18A1
Dopamine Transport
B2
MAOA
(major)
MAOB
H2O2, NH3
DOPAL
zinc, ↑ H2S, vitamin B3
B1, B3
ALDH2
DOPAC
SAM, Mg
COMT
↑ROS, RNS, aspirin, NSAIDS, oxidized fatty acids, ↑ age
Cu2, PQQ,Vit C
chronic stress, smoking, ↑ vitamin C
↑ copper, ↑ H2O2, ↓ vitamin C
DBH
PAPS
SULT1A3
Dopamine 3-O-sulfate (to urine)
↑ inflammation, summer
smoking, coffee, winter
Sodium
Norepinephrine Reuptake
SLC6A2
NOREPINEPHRINE
SLC18A1
Norepinephrine Transport
ADRB1
Norepinephrine Receptor
(minor)
(major)
SAM, Mg
COMT
SAM
PNMT
female, mental fatigue
↑ SAH, male
B2
MAOA
H2O2, NH3
ADRB1
ADRB2
ADRB3
Epinephrine Receptors
EPINEPHRINE
B2
MAOA
DOPEGAL
SAM, Mg
COMT
Adrenochrome
(major)
(minor)
Zinc
B1, B3
ADH1B
info
ALDH2
estrogen, nickel, lead
ADH6
ALDH3A2
Normetanephrine
Metanephrine
↑ vitamin C, chronic stress, ↓ inflammation
B2
MAOA
H2O2, NH3
smoking, caffeine, acute stress, male
↑ H2O2, ↑ age, ↑ vitamin C
MAOB
DHPG
DHMA
Zinc
SAM, Mg
SAM, Mg
MOPEGAL
ADH
MHPG
COMT
COMT
B3
ALDH3A2
smoking
VMA
(to urine)
Testing Key
Gene/ Enzyme
No Raw Data
Gene/ Enzyme
Checked, Nothing found
Symbols and Colors
Cofactor
Gene/ Enzyme
Increases Activity
Decreases Activity
Gene/ Enzyme
Slow
Gene/ Enzyme
Intermediate
Gene/ Enzyme
Fast
Gene/ Enzyme
Complicated
Gene/ Enzyme
info
Checked, nothing found, info available!

THE TH GENE

The TH (tyrosine hydroxylase) gene expresses an enzyme which catalyzes the conversion of L-tyrosine to dihydroxyphenylalanine (L-DOPA).

TH is mainly expressed in brain and adrenal glands, and is the rate limiting step in the synthesis of the catecholamines (dopamine, norepinephrine and epinephrine).

TH requires oxygen (O_2), iron (Fe2+) and tetrahydrobiopterin (BH4) as cofactors.

TH is dependent on the effective recycling of biopterin Biopterin Pathway.

Dirties your TH gene

Environment: Organophosphate pesticides, nickel exposure

Lifestyle: Acute and chronic stress. Limit excessive exercise which is an overlooked factor in increased oxidative stress. Avoid cigarette smoke, including secondhand smoke.

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your TH gene

Lifestyle: Stress management techniques are recommended such as meditation, breathing exercises, mindfulness, outdoor time, massage, pet therapy, moderate physical exercise.

Food: Iron, vitamins C and D rich, high fiber diet

Supplements and Medications: Consider iron, vitamin C, vitamin D, butyrate, EGCG from green tea, melatonin, *Bacopa monneri* (brahmi), *Ginkgo biloba, Panax ginseng*. Tyrosine may be useful in a low dopamine state.

- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Notable variation:

SNP: **TH 127T>C rs2070762 (+/-, AG)**

The AG genotype may be modestly upregulated compared to wild type due to lack of repressor binding site in one allele.

THE MAOA GENE

The MAOA (monoamine oxidase A) gene produces an enzyme that catalyzes the removal of an amine group from both internally-produced and externally-derived dietary and environmental amines.

Riboflavin (B2) is the required cofactor and the by-products of this reaction are hydrogen peroxide (H_2O_2) and ammonia (NH_3).

The amount of hydrogen peroxide generated by MAOA is so significant that it consumes large amounts of glutathione.

In the Dopamine Pathway, MAOA enzymes process the stress hormones dopamine, norepinephrine and epinephrine.

When MAOA performs this job, toxic levels of some substances may be created as unwelcome free riders:

- Reactive DOPAL (dihydroxyphenylacetaldehyde) when dopamine is processed.
- DOPEGAL (3,4-dihydroxyphenylglycolaldehyde), toxic to the brain, when norepinephrine is processed.
- Reactive and neurotoxic adrenochrome, when epinephrine is processed inefficiently.

If MAOA is slow (present) or COMT is slow (not present) there is also potential for neurotoxic dopamine quinone to form.

Other genes also play a role:

A slow ALDH2 (present) increases the risk of formation of toxic DOPAL and DOPEGAL. A slow ADH1B (not present) may also lead to increased DOPEGAL.

As you can see, the function of several genes influence the result of what your MAOA is doing.

Note: MAO enzymes are located on the X chromosome. Therefore, males only inherit one allele and females have inherently higher activity as a result of two X chromosomes. Males have XY chromosomes and females are XX.

MAOA activity tends to naturally increase throughout adolescence into adulthood.

Notable variation:

SNP: **MAOA T941G rs6323 (-/-, TT)**

This genotype (TT in women, T in men) lowers MAOA activity compared to G allele and may have higher dopamine levels.

Slows down your MAOA gene

Environment: Research shows a noisy sleep environment (near highway, train tracks, airports, city life, college dorms) increases catecholamine levels and workload on the MAOA enzyme. Early childhood mistreatment and maternal stress in utero have been shown to downregulate MAOA. In addition, passive exposure to smoke (even in utero) slows the MAO genes. Smoking while pregnant is associated with aggressive traits in offspring.

Lifestyle:

- Short-term, high stress situations reduce the activity of MAO enzymes presumably in order to respond to the "fight or flight" situation by reducing the break down of stress hormones.
- Iron deficiency anemia can cause a decrease in MAO activity as research indicates that insufficient levels of dietary iron in the womb can lead to poorer cognitive functioning and maladaptive social behaviors including aggressive temperament in offspring.
- Smoking (strongly) and caffeine (weakly) reduce MAO activity and raise catecholamine levels. Hence people suffering from depression often self-medicate with these substances. Using food and herbs to slow MAO (see below) may help when quitting smoking.
- Alcohol actually increases MAO activity, which is one reason why some people may use alcohol to help them relax. However, although alcohol may give an initial “relaxing” effect due to the faster processing of stress hormones, excessive or “binge” drinking can quickly overwhelm the capacity of the MAO enzymes, resulting in a build-up of damaging compounds such as dopamine quinones as well as an increased production of hydrogen peroxide which can cause neurological damage. Alcoholic beverages containing high levels of amines such as champagne and wine increase MAO workload to the greatest extent. In order to relax, MAOA activity may be regulated naturally with healthy foods and supplements (see below).

Food:

- Avoid simple, processed carbohydrates; riboflavin (B2)-deficient diet, iron-deficient diet.
- Foods containing naturally-occurring amines may reduce the capacity of MAO enzymes to degrade serotonin (an internally-produced amine). These include tyramine containing foods: aged cheeses; cured, smoked or processed meat or fish; fermented foods and sauces: yeast spreads (marmite), tempeh, miso, tamari; beer, wine and champagne; tofu and soy milk, fava beans and snow peas.
- Avoid excessive consumption of tryptophan rich foods for the same reason.

Slows down your MAOA gene, continued...

Supplements and Medications:

- Excessive tryptophan will dirty MAOA by increasing its workload and this may result in hyperactivity and sweating. Therefore, do not over supplement but use the pulse method instead.
- For those with a fast MAOA genotype that is expressing itself (or if your MAOA is acting fast due to other factors such as chronic stress or low estrogen), then these supplements may be useful to calm a fast MAOA: 5-hydroxytryptophan (5-HTP), garlic extract, berberine, curcumin, quercetin, green tea, *Rhodiola rosea*.
- Many medications interact with this enzyme, especially reversible MAO inhibitors such as pseudoephedrine, ephedrine, norephedrine. Beware concurrent use of multiple medications as MAO inhibition effects are often additive. Consult your healthcare provider or pharmacist.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Speeds up your MAOA gene

Lifestyle:

- Chronic, low-level stress causes MAO enzymes to upregulate presumably as a result of the need to break down the increased amount of stress hormones being produced.
- Low estrogen tends to raise MAOA activity. Therefore, the postpartum estrogen drop, as well as perimenopausal estrogen decline, seem to relate to upregulated MAOA levels in the brain. Fluctuations in estrogen during the menstrual cycle may contribute to mood swings through a similar relationship.
- Alcohol increases MAO activity, which reduces important neurotransmitters, and may result in both neurological and immunological deregulation. While drinking alcohol is not encouraged, if occasional alcoholic beverages are consumed then non-tyramine containing alcohols such as gin, vodka, rum, bourbon are better choices, especially if you take a MAO inhibitor.

Food: Choose iron, riboflavin (B2), vitamin C and E rich. Opt for lower amine containing foods which are low in histamine and tyramine.

Supplements and Medications: Optimize riboflavin (B2) and iron. Vitamin C, vitamin E, liposomal glutathione, S-acetyl glutathione, carnosine and PQQ (pyrroloquinoline quinone) are free radical scavengers and reduce the hydrogen peroxide produced by MAOA. It's very important to support ALDH2 and ADH1B enzymatic function as the reactive metabolites (DOPAL and DOPEGAL) generated by MAOA must be eliminated or damage may occur.

THE MAOB GENE

The MAOB (monoamine oxidase B) gene produces an enzyme that catalyzes the removal of an amine group from both internally-produced and externally-derived dietary and environmental amines and is the predominant form of MAO in the brain.

Riboflavin (B2) is the cofactor required for MAOB enzyme and the by-products of this reaction are hydrogen peroxide (H_2O_2) and ammonia (NH_3).

Significant amounts of glutathione are required to neutralize this hydrogen peroxide.

In the Dopamine Pathway, MAOB processes dopamine in the brain and central nervous system and typically this function increases as one ages, depleting dopamine and exacerbating disorders such as Parkinson's. Thus, many natural and pharmaceutical MAOB inhibitors exist to help slow MAOB and preserve dopamine.

MAO enzymes are located on the X chromosome. Therefore, males only inherit one allele and females have inherently higher activity as a result of two X chromosomes. Males have XY chromosomes and females have XX chromosomes.

Slows down your MAOB gene

Lifestyle:

- Avoid alcohol (more than one glass), caffeine (weakly inhibits), iron deficiency anemia, smoking (both active and passive exposures).
- Short-term, acute, high stress situations reduce the activity of MAOB enzymes (as response to the "fight or flight" situation by reducing the break down of stress hormones).
- Males have only one copy, so inherently possess less activity. Stress sensitive females (higher basal heart rate, lower peak estrogen and progesterone) appear to have less activity.

Food:

- Avoid simple, processed carbohydrates; riboflavin (B2)-deficient diet, iron-deficient diet.
- Foods containing naturally-occurring amines may reduce the capacity of MAO enzymes to degrade serotonin (an internally-produced amine). These include tyramine containing foods: aged cheeses; cured, smoked or processed meat or fish; fermented foods and sauces: yeast spreads (marmite), tempeh, miso, tamari; beer, wine and champagne; tofu and soy milk, fava beans and snow peas.
- Avoid excessive consumption of tryptophan rich foods for the same reason.

Notable variation:

SNP: **MAOB -36A>G rs1799836 (-/-, TT)**

The weight of evidence appears to show this variant (TT in women, T men) may be faster in the brain, but slower in other tissues of the body. Low MAOB activity in the brain (theorized C allele) would likely have higher synaptic dopamine levels in the striatal synaptic cleft while the T allele has lower dopamine levels.

Since the end products of MAO are reactive oxygen species and ammonia, the resulting levels of oxidative stress levels and cell death in the brain could be impacted by the activity of MAOB. High MAOB activity (T allele) may produce more oxidative damage and ammonia, leading to increased cell death in the brain.

Genetic contribution from just one SNP explains only a small contribution to overall gene activity. Other lifestyle factors and gene to gene interactions make up the difference in observed activity.

SNP: **MAOB 15106T>C rs5905512 (+/+, AA)**

This variant (AA in women, A in men) is not yet well studied in terms of its functional consequences. However, in diseased states, it may be upregulated. It is included here for investigational purposes in anticipation of future research that can better characterize its impact.

Slows down your MAOB gene, continued...

Supplements and Medications:

- Excessive tryptophan will dirty MAOB by increasing its workload and this may result in hyperactivity and sweating. Therefore, do not over supplement, but rather use the pulse method.
- For those with a fast MAOB genotype that is expressing itself (or your MAOB is acting fast due to other factors such as chronic stress or low estrogen), then these supplements may be useful to calm a fast MAOB: Garlic extract, berberine, curcumin, quercetin, EGCG from green tea, silymarin, *Glycyrrhiza spp.* (licorice), *Lamiaceae* (mint family: lavender, oregano, rosemary, sage, thyme, etc); *Rhodiola rosea*, *Scutellaria spp.* (skullcap), *Piper methysticum* (kava-kava), *Baptisia officinalis* (wild indigo), gentian, *Symphytum spp.* (comfrey), *Phellodendron amurense* (Amur corktree), *Cyamopsis psoralioides* (bakuchi seed), *Psoralea corylifolia* (babchi seed).
- A comprehensive list of herbs with MAOB inhibition effects can be found in Table 1 here.
- Many medications interact with this enzyme, especially reversible MAO inhibitors such as pseudoephedrine, ephedrine, norephedrine. Beware concurrent use of multiple medications as MAO inhibition effects are often additive. Consult your healthcare provider or pharmacist.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Speeds up your MAOB gene

Lifestyle:

- Long-term, low-level ongoing stress causes MAOB upregulation. MAOB activity also naturally increases with age.
- Estrogen tends to inhibit MAOB, therefore an age-related decline in estrogen is likely to further increase MAOB activity.
- Since MAOB processes dopamine in the brain and central nervous system, increased MAOB activity may cause a depletion of dopamine and exacerbate disorders such as Parkinson's.
- Alcohol increases MAOB activity, further increasing the risk of both neurological and immunological deregulation. While drinking alcohol is not encouraged, if occasional alcoholic beverages are consumed then non-tyramine containing alcohols such as gin, vodka, rum, bourbon are better choices, especially if you take a MAO inhibitor.

Food: Iron, riboflavin (B2), vitamin C and E rich

Speeds up your MAOB gene, continued...

Supplements and Medications: Optimize riboflavin (B2) and iron. Vitamin C, vitamin E, liposomal glutathione, S-acetyl glutathione, carnosine and PQQ (pyrroloquinoline quinone) are free radical scavengers and reduce the hydrogen peroxide produced by MAOA. It's very important to support ALDH2 and ADH1B enzymatic function as the reactive metabolites (DOPAL and DOPEGAL) generated by MAOA must be eliminated or damage may occur.

THE ALDH2 GENE

The ALDH2 (aldehyde dehydrogenase 2 family member) gene expresses an enzyme which converts aldehydes using the cofactor niacin (B3) for use as energy, usually in the muscle and heart.

ALDH2 also performs the role of neutralizing internally-produced lipid peroxidation products formed due to oxidative stress as well as aldehydes from the environment (see below), which put additional strain on this enzyme.

If ALDH2 enzyme is not expressing well, there is increased potential for damage in the brain caused by the reactive neurotoxic compounds, dihydroxyphenylacetaldehyde (DOPAL) and 3,4-dihydroxyphenylglycolaldehyde (DOPEGAL).

It's incredibly important to support the function of ALDH2 especially if MAOA is functioning at a faster rate (not present).

Adequate thiamine (B1) is also important.

Dirties your ALDH2 gene

Environment: Minimize exposure to aldehydes from the environment such as vehicle emissions, smoking (especially secondhand exposures), cooking fumes, formaldehyde from building materials, disinfectants, drugs, perfumes, fungicides and pesticides, carbon tetrachloride (dry cleaning), hydrogen sulfide and many other environmental chemicals. Minimize oxidative stress to decrease aldehydes created internally by reactive oxygen species.

Lifestyle: Limit alcohol, smoking, insulin resistance, oxidized LDL, high kynurenine which can all inhibit ALDH2. Work with your healthcare provider to identify *Candida* dysbiosis which generates endogenous acetaldehyde.

Notable variation:

SNP: **ALDH2 699T>C rs737280 (+/+, CC)**

This CC variant may decrease enzyme activity and makes exposures to pesticides more risky. Due to lack of research in other ethnicities, these results may be applicable only to those of European descent.

Dirties your ALDH2 gene, continued...

Food: Limit oxidized omega-6 fatty acids (from old or processed oils), known allergens, foods high in acetaldehyde such as fish products, canned vegetables, fermented foods: yogurt, vinegar, kombucha, fermented mushrooms, tempeh, miso, pickled vegetables and kimchi. Other foods containing acetaldehyde include very ripe fruit, artificial flavors like lemon flavoring, ground and instant coffee. Many aldehydes are found in drinking water so use a filter. Avoid foods and drinks containing aspartame which are metabolized to formaldehyde.

Supplements and Medications: Acetaminophen (Tylenol), aspirin

Cleans your ALDH2 gene

Environment: Employ strategies to reduce exposure to sources of acetaldehyde and other environmental chemicals.

Food: Choose vitamin B1, B3, C zinc, magnesium rich sources; especially when consuming alcohol. Opt for a diet rich in vegetables from the brassica family, broccoli sprouts.

Supplements and Medications: Thiamine (B1) is especially important as acetaldehyde damages enzymes which are B1 dependent. Consider zinc, niacin (B3), sulforaphane, resveratrol with vitamin C (especially when consuming alcohol). Some herbs have been shown in mice to speed up the biotransformation of acetaldehyde into less toxic end products. These herbs include *Lycium chinense* (goji berry), *Acanthopanax sessiliflorus*, *Ixeris dentata*, *Polypori umbellati* (zhu ling).

THE SLC18A1 GENE

The SLC18A1 (solute carrier family 18 member A1 aka VMAT1) gene expresses a membrane transport protein.

Within presynaptic neurons, SLC18A1 transports dopamine, serotonin, epinephrine and norepinephrine from the cytosol into storage vesicles. When triggered, these storage vesicles relay their stored neurotransmitters into the synaptic cleft.

The synaptic cleft is where the neurotransmitters are ready to exert their function. The neurotransmitters don't exert any effect until they bind to the receptors and carry a signal to the postsynaptic neuron. Receptor binding must take place in order for the neurotransmitter to actually function.

Cells containing the SLC18A1 transport protein are found primarily in the hypothalamus, pituitary and adrenal gland as well as the testes and gastrointestinal tract.

Chromaffin cells handle norepinephrine and epinephrine. Enterochromaffin cells store serotonin in the gastrointestinal tract.

Neurotransmitters that are not transferred into vesicles by SLC18A1 are broken down and eliminated. Therefore, if one has a fast COMT (not present) or MAOA (not present), then having a fast SLC18A1 may provide balance by increasing storage and helping to maintain an adequate level of dopamine, norepinephrine and epinephrine. However, if one has the same fast SLC18A1 but a slow COMT (not present) or MAOA (present), then, this may lead to excess neurotransmitter accumulation in the presynaptic neuron, resulting in symptoms of excess neurotransmitters. This is especially the case if the postsynaptic receptors are also increased.

It's important to evaluate the incoming production of dopamine, norepinephrine and epinephrine (TH, DDC, DBH, PNMT, GCH1) while also evaluating the receptor activity (DRDs, ARDBs) and re-uptake of neurotransmitters out of the synaptic cleft (SLC6A2, SLC6A3) along with understanding the elimination of neurotransmitters (COMT, MAOA, MAOB, ADH, ALDH). This is yet another reason why one must examine the entire process of how neurotransmitters function versus the impact of SNPs in isolation.

Notable variation:

SNP: **SLC18A1 C407T rs1390938 (+/-, AG)**

This AG variant represents an intermediate state between a higher transport activity conferred by the homozygous (AA) genotype and lesser activity conferred by the absence of the A allele (GG genotype). Thus, GG<AG<AA.

The resulting intermediate neurotransmitter levels appear to decrease prefrontal cortex function while increasing amygdala reactivity compared to GG. Research evidence suggests the more robust amygdala reactions of AG compared to GG may represent enhanced resilience against negative life stress and low moods.

A-allele carriers appear to show less maladaptive impulsivity, nervousness, low moods, and neuroticism. They were less likely to have been diagnosed with an affective and/or alcohol use disorder by young adulthood. A carriers appear less likely to develop negative emotionality: aggression, alienation, and stress reactivity. They exhibit less severe alcohol withdrawal symptoms compared to GG. In other studies, G allele carriers showed increased risk of being on the spectrum of autism. They demonstrate alternating high and low moods. Note: Due to lack of research in other ethnicities, these observations may be applicable only to those of European descent.

This particular SNP is a special case. Both A and G alleles are major in some ethnicities. This implies they both have evolutionary advantage given how the environment (latitude, altitude, disease pressure, nutrition, etc) shaped their selection.

Dirties your SLC18A1 gene

Environment: Environmental chemicals including polychlorinated biphenyls (PCBs) and organochlorine pesticides have been shown to inhibit SLC18A1 activity and deplete dopamine stores in experimental animals. Exposure to organochlorines may be associated with an increased incidence of Parkinson's disease.

Food: Avoid organochlorine pesticides in food; see the Dirty Dozen as explained by Environmental Working Group.

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your SLC18A1 gene

Lifestyle: Acute and chronic stress management techniques are recommended such as meditation, breathing exercises, mindfulness, outdoor time, massage, pet therapy, moderate physical exercise.

Food: Consume organic fruits, organic vegetables, organic grain and organic dairy products whenever possible. Prioritize your food dollars by knowing the Clean 15 as explained by Environmental Working Group.

Supplements and Medications: *Ginkgo biloba* has been found to regulate various dopamine genes (in mice) including SLC18A1 and reduce neurotoxicity caused by environmental chemicals. Lithium orotate may be considered especially if experiencing a slow COMT and/or slow MAOA. To determine your status, do the quizzes in the Dirty Genes book. Work with your healthcare provider in order to identify and correct underlying neurotransmitter imbalances.

THE DRD2 GENE

The DRD2 (dopamine receptor D2) gene expresses a protein that functions as a receptor for dopamine. Dopamine is a key neurotransmitter that regulates a variety of physiological functions. Dopamine supports reward behavior, regulation of movement, attention, learning, and memory.

DRD2 receptors regulate the release, uptake, and synthesis of dopamine via the feedback process known as “auto-inhibition”. Think of auto-inhibition as how a person modulates the volume of their speaking voice based on their environment. Neurons adjust dopamine levels based on the concentration of dopamine that they sense binding to dopamine D2 receptors on a cell surface.

Two isoforms, or types, of the D2 receptor, are known to exist. Details of their different roles are not well understood.

D2S (short) is found on presynaptic neurons and regulates the levels of dopamine within the synaptic cleft. Lower expression of D2S results in reduced auto-inhibition and thus higher levels of dopamine.

The D2L (long) is found on postsynaptic neurons. The activation of D2L receptors causes enhanced signaling in the dopamine-dependent pathways.

Dirties your DRD2 gene

Environment: Bisphenol A (BPA), welding fumes and formaldehyde

Food: Low iron reduces DRD2 receptor density

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your DRD2 gene

Lifestyle: Exercise, cognitive behavior therapy or psychotherapy

Food: Iron rich foods

Supplements and Medications: Optimize riboflavin (B2) and iron. Consider inositol. Vitamin C, vitamin E, liposomal glutathione, S-acetyl glutathione, carnosine and PQQ (pyrroloquinoline quinone) are free radical scavengers and reduce the hydrogen peroxide produced by MAO.

Notable variation:

SNP: **DRD2 Taq1A rs1800497 (+/-, AG)**
GA carriers have 15-20% less D2 receptor binding potential compared to wild type. This variant may increase risk of mood disorders, inattention, over-reliance on pain killers and adverse reactions to stress.

SNP: **DRD2 -1189T>C rs12364283 (-/-, AA)**
This AA wild type may have decreased receptor density by 5-30% compared to either of the variants. The rs12364283 AA genotype was associated with personality changes including poorer behavioral inhibition and increased impulsivity possibly via inhibition of neurotransmission.

SNP: **DRD2 -83G>T rs1076560 (+/-, AC)**
This CA variant is associated with reduced expression and fewer presynaptic DRD2-short receptors relative to a higher number of postsynaptic DRD2-long receptors. This change results in higher levels of dopamine in the synaptic cleft compared to wild-type CC. This causes lower performance with focus, cognition, and attentional tasks. A allele carriers either took longer completing a task with multiple steps or functional MRI showed greater energy expenditures for similar task performance. A allele carriers may experience a deterioration in mood from irritating noise and may experience better cognition in quiet environment. In addition, A allele carriers may exhibit increased susceptibility to dependency on substances.

Note: rs1076560 and rs2283265 are always inherited together in all populations. Research for the minor allele of rs2283265 would reflect the same results as the minor allele for rs1076560 and vice-versa.

THE SLC6A3 GENE

The SLC6A3 (solute carrier family 6 member 3 aka DAT1) gene expresses a re-uptake transporter for dopamine.

SLC6A3 transports dopamine out of the synaptic cleft and back into the presynaptic neuron thus reducing dopamine activity. Within the presynaptic neuron, other transporters then sequester the dopamine into vesicles for storage and later release.

Dopamine plays a role in reward-motivated behavior and the rate at which SLC6A3 removes dopamine from the synapse can have a profound effect on the amount of dopamine in the cell.

SLC6A3 works by coupling the transport of dopamine into the cell with the flow of sodium and chloride ions into the cell, from high to low concentration. Two sodium and one chloride ions are transported by SLC6A3 along with the dopamine substrate.

Dirties your SLC6A3 gene

Environment: Welding fumes, bisphenol A (BPA), pesticides (especially paraquat), polychlorinated biphenyls (PCBs), gram negative infections (especially Lyme)

Lifestyle: Nicotine, cocaine; hostile, aggressive situations; absence of maternal affection, low positive social connection

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your SLC6A3 gene

Lifestyle: Create warm and reinforcing interactions that would promote or reward prosocial behavior, strong social ties with friendly peers, positive measures to negotiate conflicts or disagreements.

Food: Iron rich, vitamin A, high levels of butyrate (short chain fatty acids), high fiber diet

Supplements and Medications: *Ginkgo biloba*, N-acetylcysteine (NAC) increases dopamine binding to the transporter.

Notable variation:

SNP: **SLC6A3 1215A>G rs6347 (+/-, TC)**

This TC variant appears to slightly increase expression of SLC6A3 (DAT1). The C allele results in lower synaptic dopamine levels as a consequence of increased numbers of re-uptake transporters. This variant may slightly increase the risk of impaired cognition in old age.

THE COMT GENE

The COMT (catechol-O-methyltransferase) gene expresses a phase II enzyme which degrades and inactivates catechol-containing compounds such as the catecholamines (dopamine, epinephrine, and norepinephrine), catechol estrogens, and various drugs and substances that have a catechol structure. Magnesium is needed for the reaction.

COMT acts by catalyzing the transfer of a methyl group from S-adenosylmethionine (SAM), resulting in the generation of S-adenosylhomocysteine (SAH). A build-up of SAH inhibits SAM binding and reduces COMT activity.

Genetic variants that decrease the activity of COMT can lead to elevations in 4-hydroxy-estrogens, which have been shown to damage DNA and have carcinogenic potential.

If COMT enzyme is functioning slowly, there is also more potential for the neurotoxic compound dopamine quinone to form, especially in the presence of other reactive oxygen species.

If both COMT and MAOA are functioning slowly, there is more potential for neurotoxic adrenochrome to form.

A faster COMT enzyme may be more protective against the reactive neurotoxic compounds of dopamine quinone and adrenochrome, however higher levels of COMT activity result in the depletion of levels of dopamine and norepinephrine.

Dirties your intermediate speed COMT gene

Environment: Research shows a noisy sleep environment (near highway, train tracks, airports, city life, college dorms) increases catecholamine levels and workload on the COMT enzyme thereby making this balanced haplotype into a slow COMT. Infections may imbalance this otherwise balanced haplotype leading to a fast COMT.

Lifestyle: Traumatic brain injury, lack of exercise, low oxygen to tissues all slow COMT. A routine lifestyle may add comfort but, long term, it may lead to boredom; while a fast-paced lifestyle may lead to burn-out.

Food: A diet high in processed carbohydrates and low protein intake can be detrimental to this intermediate type. This is potentially amplified by a faster MAOA (not present) and a slower DRD2 (present). Opt for balanced meals with moderate protein. Diets that focus heavily on one macronutrient such as high fat ketogenic type diets or high protein Paleo/GAPS type diets or even fasting may be tolerated intermittently but not long-term.

Notable variation:

An Intermediate COMT Haplotype

Your COMT haplotype pattern is calculated as INTERMEDIATE. This combination confers average COMT activity and average pain sensitivity.

Note: Your raw data file is missing at least one SNP of the 4 SNP haplotype utilized to determine COMT speed. Therefore your COMT speed is based on a combination of 2 SNPs and is slightly less accurate than the 4 SNP determination used in research models. If this contradicts results gleaned from previous genomic testing see this FAQ for an explanation.

In vivo analysis of this combination indicates a moderate 2.5 to 3-fold reduction in enzymatic activity compared to the high activity haplotype. Although you were born with this genotypic intermediate speed for COMT, it does not mean that it functions at an intermediate speed all the time. In fact, it fluctuates many times a day. Your lifestyle, foods, environment, supplements and medications easily influence COMT to function faster or slower.

If your COMT is working too fast, you may experience symptoms of depression, lack of motivation, increased addictive tendencies, poor concentration and learning difficulties. If your COMT is working too slow, you may experience symptoms of anxiety, irritability, difficulty falling asleep, significant PMS, migraines, headaches and increased cardiovascular risk. The key is knowing how your daily choices influence your COMT. Then you can learn to keep it balanced. Refer to *Dirty Genes* quizzes to see how your COMT and MAOA are expressing.

Gene	rsID	Alias	Variant Allele	Call
COMT	rs6269	-98A>G	G	AA
COMT	rs4680	V158M	A	AA

Dirties your intermediate speed COMT gene, continued...

Supplements and Medications: Carriers of this well-balanced haplotype may get out of balance with medications and supplements. Following a long term supplement or medication plan that is rigid (e.g., Take X supplement morning and night) may work in the short term, but long term may cause side effects. Use the 'pulsing' method as described in the *Dirty Genes* book.

Cleans your intermediate speed COMT gene

Lifestyle: Be mindful that your lifestyle choices may speed up or slow down your COMT haplotype. It's very important that you're aware how your daily choices and activities are affecting your COMT expression. In general, balance in everything is key to maintaining an optimally functioning COMT. Excess or deficiency can push one to a slow or fast COMT. You must learn the symptoms of both a Fast COMT and Slow COMT in *Dirty Genes* as you will switch back and forth. At first, this will be a steep learning curve but once you get it, it will greatly help optimize your life.

Food: Having a more varied diet depending on your activities and moods is very important. Take the quizzes in the book, *Dirty Genes*, to see where you are at the moment here. Learn the food recommendations for both a Fast COMT and Slow COMT and eat to nourish the one that needs balance. Use recipes in the *Dirty Genes* book to get you started.

Supplements and Medications: It's important to understand which supplements may speed up or slow down the COMT gene. Read about this in Dirty Genes, take the quizzes and see where you are at the moment. Use the Pulse Method as defined in *Dirty Genes* to prevent side effects from taking supplements and medications rigidly on a long-term basis. Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

THE ADRB1 GENE

ADRB1 (adrenoceptor beta 1) gene expresses receptors for epinephrine and norepinephrine.

The three subtypes of ADRB, β1, β2, β3, are located primarily in the central nervous system (CNS), heart, coronary artery, kidney and muscle.

ADRB receptors are involved in development, behavior, smooth muscle tone, heart function, and energy metabolism.

All three β-subtypes also coexist in both white and brown adipose tissue. In white adipose tissue, attachment of epinephrine and norepinephrine to the ADRB receptors is thought to stimulate lipolysis (the release of fat stores for fuel) in response to fasting, whereas in brown adipose tissue, they stimulate heat production in response to cold exposure or overfeeding.

ADRB1 binds epinephrine and norepinephrine with approximately equal affinity.

Dirties your ADRB1 gene

Environment: Coercive, hostile or aggressive situations; low positive social connection

Lifestyle: Thyroid dysregulation (both hypo and hyperthyroidism)

Cleans your ADRB1 gene

Lifestyle: Create warm and reinforcing interactions that would promote or reward prosocial behavior, strong social ties with friendly peers, positive measures to negotiate conflicts or disagreements.

Notable variation:

SNP: **ADRB1 1165G>C rs1801253 (-/-, CC)**
This CC variant is more sensitive to stimulation from its agonists: epinephrine and norepinephrine.

THE ADRB2 GENE

ADRB2 (adrenoceptor beta 2) gene expresses receptors for epinephrine and norepinephrine.

The three subtypes of ADRB: β1, β2, β3, are located primarily in the central nervous system (CNS), heart, coronary artery, kidney and muscle.

ADRB receptors are involved in development, behavior, smooth muscle tone, heart function, and energy metabolism.

All three β-subtypes also coexist in both white and brown adipose tissue. In white adipose tissue, attachment of epinephrine and norepinephrine to the ADRB receptors is thought to stimulate lipolysis (the release of fat stores for fuel) in response to fasting, whereas in brown adipose tissue, they stimulate heat production in response to cold exposure or overfeeding.

ADRB2 binds epinephrine with an approximately 30-fold greater affinity than norepinephrine.

Dirties your ADRB2 gene

Environment: Coercive, hostile or aggressive situations; low positive social connection

Lifestyle: Thyroid dysregulation (both hypo and hyperthyroidism)

Cleans your ADRB2 gene

Lifestyle: Create warm and reinforcing interactions that would promote or reward prosocial behavior, strong social ties with friendly peers, take positive measures to negotiate conflicts or disagreements.

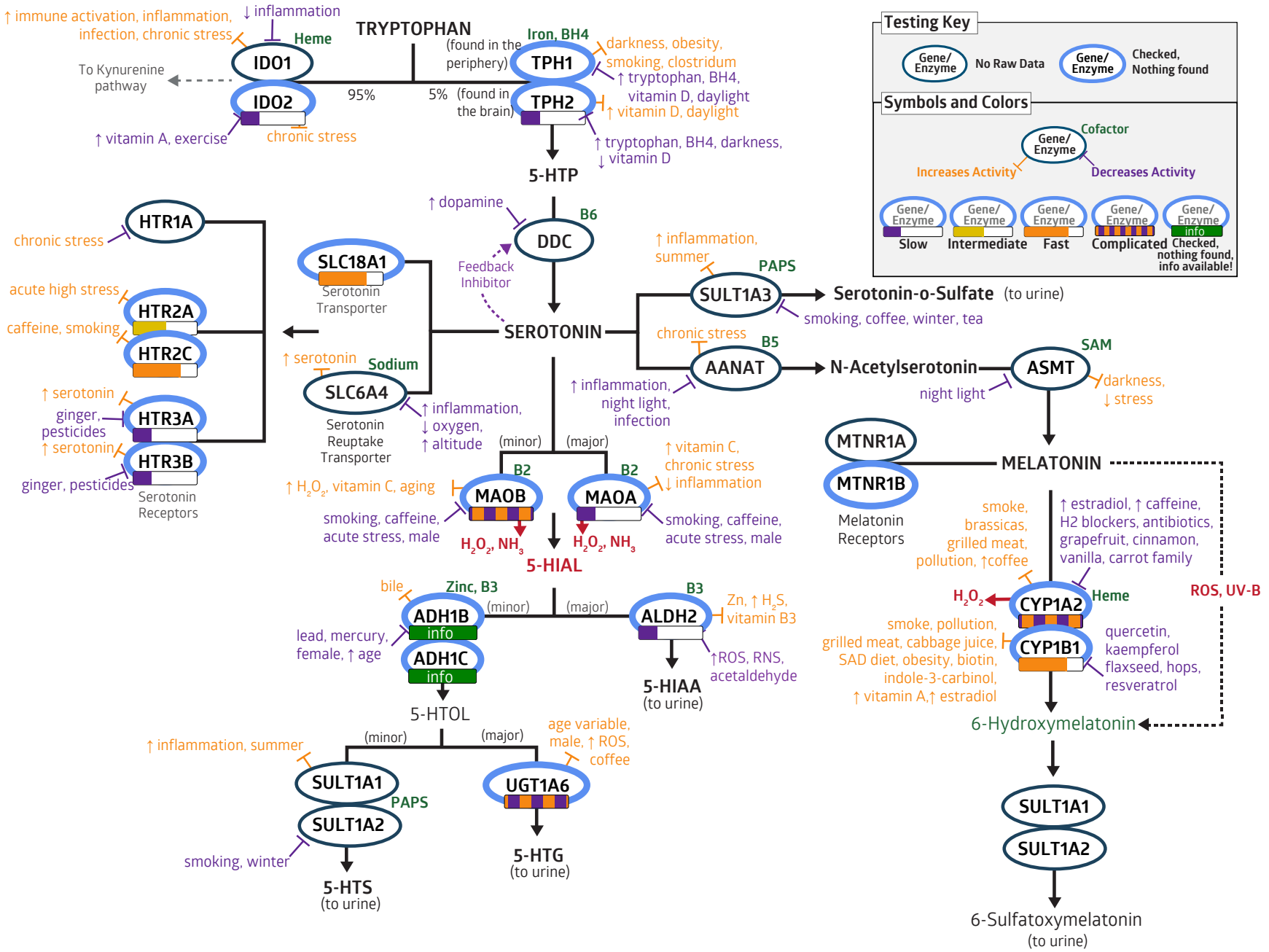
THE ADH1B/1C GENE

The complete discussion of this gene is under Serotonin.

Notable variation:

SNP: **ADRB2 5285A>G rs1042713 (+/+, AA)**
This AA variant results in blunted receptor function compared with the receptor function of GG wildtype. The AA genotype shows less vasodilation in response to the endogenous beta-agonists epinephrine and norepinephrine. AA carriers saw improved lipid markers with high physical activity defined by >5,000 steps/day.

SNP: **ADRB2 79C>G rs1042714 (-/-, CC)**
This CC (wild type) showed enhanced receptor function with better smooth muscle relaxation and improved vasodilation in response to binding of epinephrine and norepinephrine compared with GG variant.


↑ immune activation, inflammation, infection, chronic stress
↓ inflammation
Heme
IDO1
To Kynurenine pathway
IDO2
↑ vitamin A, exercise
chronic stress
TRYPTOPHAN
95%
5%
(found in the periphery)
(found in the brain)
Iron, BH4
TPH1
TPH2
darkness, obesity, smoking, clostridum
↑ tryptophan, BH4, vitamin D, daylight
↑ vitamin D, daylight
↑ tryptophan, BH4, darkness, ↓ vitamin D
5-HTP
↑ dopamine
B6
DDC
Feedback Inhibitor
SEROTONIN
HTR1A
chronic stress
HTR2A
acute high stress
caffeine, smoking
HTR2C
↑ serotonin
ginger, pesticides
↑ serotonin
HTR3A
HTR3B
ginger, pesticides
Serotonin Receptors
SLC18A1
Serotonin Transporter
↑ serotonin
Sodium
SLC6A4
Serotonin Reuptake Transporter
↑ inflammation, ↓ oxygen, ↑ altitude
(minor)
(major)
B2
B2
↑ H2O2, vitamin C, aging
MAOB
MAOA
smoking, caffeine, acute stress, male
H2O2, NH3
H2O2, NH3
smoking, caffeine, acute stress, male
↑ vitamin C, chronic stress ↓ inflammation
5-HIAL
↑ inflammation, summer
PAPS
SULT1A3
Serotonin-o-Sulfate (to urine)
smoking, coffee, winter, tea
chronic stress
B5
AANAT
↑ inflammation, night light, infection
N-Acetylserotonin
SAM
ASMT
night light
darkness, ↓ stress
MTNR1A
MTNR1B
Melatonin Receptors
MELATONIN
smoke, brassicas, grilled meat, pollution, ↑coffee
↑ estradiol, ↑ caffeine, H2 blockers, antibiotics, grapefruit, cinnamon, vanilla, carrot family
H2O2
CYP1A2
Heme
ROS, UV-B
smoke, pollution, grilled meat, cabbage juice, SAD diet, obesity, biotin, indole-3-carbinol, ↑ vitamin A,↑ estradiol
CYP1B1
quercetin, kaempferol flaxseed, hops, resveratrol
6-Hydroxymelatonin
SULT1A1
SULT1A2
6-Sulfatoxymelatonin
(to urine)
bile
Zinc, B3
ADH1B
info
ADH1C
info
lead, mercury, female, ↑ age
(minor)
(major)
B3
ALDH2
Zn, ↑ H2S, vitamin B3
↑ROS, RNS, acetaldehyde
5-HIAA
(to urine)
5-HTOL
↑ inflammation, summer
(minor)
(major)
age variable, male, ↑ ROS, coffee
SULT1A1
SULT1A2
PAPS
smoking, winter
5-HTS
(to urine)
UGT1A6
5-HTG
(to urine)
Testing Key
Gene/ Enzyme
No Raw Data
Gene/ Enzyme
Checked, Nothing found
Symbols and Colors
Gene/ Enzyme
Cofactor
Increases Activity
Decreases Activity
Gene/ Enzyme
Slow
Gene/ Enzyme
Intermediate
Gene/ Enzyme
Fast
Gene/ Enzyme
Complicated
Gene/ Enzyme
info
Checked, nothing found, info available!

THE IDO2 GENE

The IDO2 (Indoleamine 2,3-dioxygenase 2) gene expresses an enzyme which catalyzes the first and rate-limiting step in the conversion of tryptophan to kynurenine using heme as a cofactor. (The affinity of IDO2 for tryptophan is much lower than that of IDO1.)

Tryptophan is required by T lymphocytes for cell division and proliferation. Therefore, IDO plays an important role in modulating T-cell behavior by controlling the amount of tryptophan available.

Depletion of tryptophan, via increased IDO activity, promotes immune tolerance, helps to prevent autoimmunity and is important in pregnancy for preventing rejection of the fetus. However, excessive depletion of tryptophan, due to upregulation of IDO can result in the suppression of T cells and natural killer (NK) cells.

A suppressed immune system increases the risk of opportunistic bacterial, fungal, parasitic, viral infections and cancer, especially in the immunocompromised. This is known as 'Immune Escape.'

Additionally, upregulated IDO2 may enhance pain sensitivity because tryptophan metabolites produced by IDO are irritants to the nervous system.

Dirties your IDO2 gene

Environment: Work with your healthcare provider to identify and treat any infections, as evidenced by increased susceptibility to opportunistic infections such as *Candida spp., Aspergillus spp.,* Lyme, Herpes or Epstein-Barr virus. Pay attention to indoor air quality of home, school or workplace, especially if history of water damage and potential for mold exposures. Avoid industrial pollution, dioxins.

Lifestyle:

- Excessive exercise, and/or chronic low level stress.
- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage as heme is the required cofactor for this enzyme. Many parasites and gram negative bacteria need the iron-containing cofactor, heme, to reproduce and cause infection. Parasites and bacterial pathogens must synthesize their own heme or acquire heme from the host. Thus, untreated chronic parasites and bacterial infections may create a heme deficiency. Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.

Notable variation:

SNP: **IDO2 R248W rs10109853 (+/-, TC)**

This CT variant in viral and T-cell response studies indicate activity is 50% of wild type. This may increase susceptibility to autoimmune conditions but may improve immune defense against opportunistic bacterial, fungal, parasitic or viral infections.

Dirties your IDO2 gene, continued...

Food: Avoid diet high in fat (>60% of calories), fatty meats and animal fats such as butter or lard which concentrate dioxins; the standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium, oxidized inflammatory fats, and low in fiber and good quality protein.

Supplements and Medications: Consider *Saccharomyces boulardii* while taking antibiotics and pay attention to probiotics after an antibiotic course due to increased susceptibility to *Candida* dysbiosis. Avoid proton pump inhibitor drugs (Prilosec, Prevacid, Nexium). Many other medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your IDO2 gene

Environment: Use an extractor hood while cooking and high-smoke point oils like ghee or avocado oil.

Lifestyle: Stress management techniques are recommended such as meditation, breathing exercises, mindfulness, outdoor time, massage, pet therapy, moderate physical exercise.

Food: Focus on vitamin A, beta carotene and heme-iron rich sources. Studies show that appropriate levels of vitamin A help to balance IDO activity and support production of T cells and natural killer (NK) cells. Opt for a diet rich in cruciferous vegetables.

Supplements and Medications: Optimizing levels of iron and vitamin A is important but high levels taken long term may have negative consequences. Always strive to obtain these nutrients from food sources first and follow the pulse method when supplementing, as described in the *Dirty Genes* book. Seek guidance from a qualified health professional. Optimize niacin (B3).

THE TPH2 GENE

The TPH2 (tryptophan hydroxylase 2) gene expresses an enzyme which catalyzes the initial, rate-limiting step in the production of the neurotransmitter serotonin. This process requires oxygen (O_2), iron (Fe2+) and tetrahydrobiopterin (BH4) as cofactors. TPH2 is dependent on the recycling of biopterin (see biopterin recycling pathway).

Whereas TPH1 is mainly expressed in peripheral tissues such as the skin and gut, TPH2 is exclusively expressed in neuronal cells in the brain and central nervous system. Although 90% of the body's serotonin production is generated by TPH1 in the gut, this serotonin cannot pass the blood-brain barrier into the brain. Therefore, TPH2 is responsible for the majority of brain-generated serotonin.

Serotonin generated in peripheral tissues by THP1 is involved in the regulation of gut motility and vascular tone, while serotonin generated in the brain by TPH2 is involved more in the regulation of mood, confidence and wakefulness. The exception to this is that TPH1 is found in the pineal gland in the brain and is actually there at levels some 150 times higher than TPH2. This may be due to the need to generate melatonin in the pineal gland brain at night, while serotonin in other parts of the brain is low.

Vitamin D has been found to have an opposite effect on the two enzymes. Vitamin D activates the transcription of TPH2 in the brain and represses the transcription of TPH1 in tissues outside the blood-brain barrier.

Vitamin D naturally follows a diurnal rhythm, with lower levels at night, rising to a maximum at around midday. This provides the body with a mechanism to control the level of serotonin generated in the brain: with higher levels of vitamin D during daylight hours activating TPH2 to increase serotonin in the brain and increase wakefulness, while lower levels of vitamin D at night reduces serotonin in the brain and reduces stimulation. Vitamin D also fluctuates seasonally, with generally lower levels observed during the winter months. This may be one explanation for the Seasonal Affective Disorder (SAD) suffered by people who are not exposed to sufficient daylight.

Dirties your TPH2 gene

Environment: Pay attention to indoor air quality of home, kitchen, airport, school or workplace, especially if history of water damage and potential for mold exposures.

Lifestyle: Minimize coercive, hostile or aggressive situations, low positive social connection, early life stresses. Living in northern latitudes and/or shiftwork will reduce exposure to natural daylight and reduce TPH2 activation in the brain.

Notable variation:

SNP: **TPH2 G-703T rs4570625 (-/-, GG)**

This GG wild type has lower serotonin production compared to variants. Carriers of this wild type form may therefore have reduced serotonergic transmission and lower amygdala activation. Research evidence suggests that lower amygdala activation may represent reduced resilience against negative life stress and low moods.

Dirties your TPH2 gene, continued...

Food: Low tryptophan containing meals may reduce the amount of available tryptophan for TPH2 to function. Conversely, high protein meals such as GAPS and Paleo may reduce tryptophan from entering the brain.

Supplements and Medications: Pay attention to probiotics after an antibiotic course as dysbiosis decreases intestinal serotonin levels.

Cleans your TPH2 gene

Environment: Use an extractor hood while cooking and high-smoke point oils such as ghee or avocado oil.

Lifestyle:

- Stress management techniques are recommended such as meditation, breathing exercises, mindfulness, outdoor time, massage, pet therapy, moderate physical exercise.
- Create warm and reinforcing interactions that would promote or reward prosocial behavior, strong social ties with friendly peers.

Food: Choose iron, vitamin D, folate rich foods. A balanced meal with protein and carbohydrate may increase tryptophan delivery in the brain. Ketogenic diet (high fat with some protein) also appears to deliver tryptophan quite effectively to the brain which may be one of the mechanisms of how the ketogenic diet helps those with seizures.

Supplements and Medications:

- Consider 5-HTP, vitamin D, iron, niacin (B3).
- Optimize BH4 levels with sufficient folinic acid, antioxidants like liposomal glutathione, PQQ and vitamin C.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

THE SLC18A1 GENE

The complete discussion of this gene is under Dopamine.

THE HTR2A GENE

The HTR2A (5-hydroxytryptamine receptor 2A) gene expresses a receptor for serotonin found in various parts of the brain, central and peripheral nervous system as well as platelets, cardiovascular and gastrointestinal tissue.

In addition to serotonin, HTR2A receptors also function as receptors for various drugs and psychoactive substances.

HTR2A receptors also play a role in behavior, memory, learning, intestinal smooth muscle contraction and platelet aggregation.

Dirties your HTR2A gene

Lifestyle: Acute stress, secondhand smoke, dehydration

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your HTR2A gene

Lifestyle:

- Optimize hydration by drinking water with appropriate electrolyte balance. Hydration is not just drinking water but the process of causing something to absorb water. Electrolytes enhance water absorption inside cells.
- Acute stress management techniques are recommended such as breathing exercises, cognitive reframing (choosing a different way to perceive the situation), progressive muscle relaxation.

Food: Foods rich in calcium and omega-3 fatty acids alpha-linolenic acid (ALA) and docosahexaenoic acid (DHA).

Supplements and Medications: Consider myo-inositol, N-acetylcysteine (NAC), alpha lipoic acid, calcium, omega-3 fish oils.

Notable variation:

SNP: **HTR2A G-1438A rs6311 (+/-, TC)**

This CT variant appears to increase the expression of HTR2A serotonin receptors, resulting in increased serotonin binding and enhanced serotonergic activity relative to CC, although not as much as TT carriers. The T allele has been associated with obsessiveness and persistent fatigue.

THE HTR2C GENE

The HTR2C (5-hydroxytryptamine receptor 2C) gene expresses a receptor found in the choroid plexus of the brain for 5-hydroxytryptamine (serotonin).

Activation of this receptor increases dopamine and norepinephrine secretion in various areas of the brain and helps regulate appetite, mood and sexual response.

The HTR2C receptor is also an important regulator of the hypothalamus-pituitary-adrenal (HPA) axis via its interactions with prolactin, oxytocin and vasopressin.

HTR2C resides on the X chromosome, so males have one copy, while females have two.

Dirties your HTR2C gene

Environment: Prenatal androgen exposure (such as during polycystic ovarian syndrome pregnancies) may affect fetal brains making female brains more masculinized.

Lifestyle: Minimize psychosocial stressors, prolonged intense exercise, dehydration, caffeine, smoking.

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your HTR2C gene

Lifestyle: Optimize hydration by drinking water with appropriate electrolyte balance. Hydration is not just drinking water but the process of causing something to absorb water. Electrolytes enhance water absorption inside cells.

Food: Foods rich in calcium and omega-3 fatty acids alpha-linolenic acid (ALA) and docosahexaenoic acid (DHA).

Supplements and Medications: Consider 5-hydroxytryptophan (5-HTP), curcumin, *Hypericum perforatum* (St. John's wort), *Bacopa monnieri* (brahmi), omega-3 fish oils. Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Notable variation:

SNP: **HTR2C C759T rs3813929 (+/+, TT)**

This variant (TT in women, T- in men) is approximately 150% more transcriptionally active compared to wild type and expresses more receptors on neuronal surfaces. This may be protective against weight gain from psychotropic medications and reduces susceptibility to inattention.

THE HTR3A GENE

The HTR3A (5-hydroxytryptamine receptor 3A) gene expresses a receptor for 5-hydroxytryptamine (serotonin) that differs structurally and functionally from all other serotonin receptors.

The 5-HT3 receptors are found throughout the central and peripheral nervous system and are activated by many compounds beyond serotonin, such as local and general anesthetics.

5-HT3 receptors in the CNS may play roles in a variety of functions including vomiting, cognition, anxiety and regulation of the reward system.

Dirties your HTR3A gene

Environment: Avoid organochlorine pesticides in food; see the Dirty Dozen as explained by Environmental Working Group.

Lifestyle: Adverse life events (abuse, neglect, poverty, discrimination); nicotine, alcohol.

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your HTR3A gene

Environment: Create warm and reinforcing interactions that would promote or reward prosocial behavior. Create strong social ties with friendly peers.

Lifestyle: Create safe, nurturing home and school environment. Take measures to negotiate and resolve conflicts or disagreements, seek conflict resolution, practice reframing techniques (how one chooses to respond to a situation) and mindfulness. Consider psychotherapy, acupuncture, homeopathy for past trauma. Stress management techniques are recommended such as meditation, breathing exercises, mindfulness, outdoor time, massage, pet therapy, moderate physical exercise.

Food: Choose serotonin-rich foods. Consume organic fruits, organic vegetables, organic grain and organic dairy products whenever possible. Prioritize your food dollars by knowing the Clean 15 as explained by Environmental Working Group.

Supplements and Medications: 5-hydroxytryptophan (5-HTP). Ginger is effective in reducing feelings of nausea caused by motion, pregnancy or chemotherapy.

Notable variation:

SNP: **HTR3A C178T rs1062613 (-/-, CC)**

This CC wild type has lower expression and fewer receptors on the cell surface as compared to TT. In addition, carriers of this CC wild type have approximately 30% lower 5-hydroxyindoleacetic acid (5-HIAA) levels in the cerebrospinal fluid. 5-HIAA is the main metabolite of serotonin, suggesting that 5-HT3A-containing receptors regulate the serotonin turnover rates in the central nervous system. Researchers observed CC individuals are more susceptible to decreased serotonin receptor expression caused by childhood stressors occurring at a very young age, or while in utero. C allele is also associated with nervousness and pessimism, shyness, fearfulness and doubt.

THE HTR3B GENE

The HTR3B (5-hydroxytryptamine receptor 3B) gene expresses a receptor for 5-hydroxytryptamine (serotonin) that differs structurally and functionally from all other serotonin receptors.

The 5-HT3 receptors are found throughout the central and peripheral nervous system and are activated by many compounds beyond serotonin, such as local and general anesthetics.

5-HT3 receptors in the CNS may play roles in a variety of functions including vomiting, cognition, anxiety and regulation of the reward system.

Dirties your HTR3B gene

Environment: Avoid organochlorine pesticides in food; see the Dirty Dozen as explained by Environmental Working Group.

Lifestyle: Adverse life events (abuse, neglect, poverty, discrimination), nicotine, alcohol.

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your HTR3B gene

Environment: Create warm and reinforcing interactions that would promote or reward prosocial behavior. Create strong social ties with friendly peers.

Lifestyle: Create safe, nurturing home and school environment. Take measures to negotiate and resolve conflicts or disagreements, seek conflict resolution, practice reframing techniques (how one chooses to respond to a situation) and mindfulness. Consider psychotherapy, acupuncture, homeopathy for past trauma. Stress management techniques are recommended such as meditation, breathing exercises, mindfulness, outdoor time, massage, pet therapy, moderate physical exercise.

Food: Choose serotonin-rich foods. Consume organic fruits, organic vegetables, organic grain and organic dairy products whenever possible. Prioritize your food dollars by knowing the Clean 15 as explained by Environmental Working Group.

Supplements and Medications: 5-hydroxytryptophan (5-HTP). Ginger is effective in reducing feelings of nausea caused by motion, pregnancy or chemotherapy.

Notable variation:

SNP: **HTR3B A386C rs1176744 (-/-, AA)**

This AA wild type causes a significant decrease in single-channel mean open time compared with homozygous CC types. This represents a significant decrease in receptor signaling to serotonin and is thought to be potentially deleterious. The A allele has been associated with low mood, pain sensitivity. The A allele is also associated with irregular high and low moods, unhealthy response to perceived body weight, and very low mood. Conversely, by virtue of its reduced serotonin response, the A allele appears to decrease nervousness.

THE MAOA GENE

The MAOA (monoamine oxidase A) gene produces an enzyme that catalyzes the removal of an amine group from both internally-produced and externally-derived dietary and environmental amines. Riboflavin (B2) is the required cofactor and the by-products of this reaction are hydrogen peroxide (H_2O_2) and ammonia (NH_3).

The amount of hydrogen peroxide generated by MAOA is so significant that it consumes significant amounts of glutathione.

In the Serotonin Pathway, MAO enzymes process and detoxify the neurotransmitter serotonin. In all of these reactions, MAOA represents the major route, and MAOB the minor route. Serotonin is a neurotransmitter that helps us feel at peace, optimistic, and self-confident. However, serotonin can easily become dysregulated. Low levels of serotonin can cause anxiety, depression, cravings and insomnia. High levels of serotonin can also cause anxiety (this time associated with irritability rather than depression), as well as rapid heart rate, high blood pressure and a host of other symptoms.

MAO enzymes are located on the X chromosome. Therefore, males only inherit one allele and females have inherently higher activity as a result of two X chromosomes.

Slows down your MAOA gene

Environment:

- Research shows that a noisy sleep environment (near highway, train tracks, airports, city life, college dorms) increases catecholamine levels and workload on the MAOA enzyme.
- Early childhood mistreatment and maternal stress in utero have been shown to downregulate MAOA.
- Passive exposure to smoke (even in utero) slows the MAO genes. Smoking while pregnant is associated with aggressive traits in offspring.

Notable variation:

SNP: **MAOA T941G rs6323 (-/-, TT)**
This genotype (TT in women, T in men) lowers MAOA activity and may exhibit higher levels of serotonin.

Slows down your MAOA gene, continued...

Lifestyle:

- Short-term, high stress situations reduce the activity of MAO enzymes presumably in order to respond to the "fight or flight" situation by reducing the break down of stress hormones.
- Iron deficiency anemia can cause a decrease in MAO activity as research indicates that insufficient levels of dietary iron in the womb can lead to poorer cognitive functioning and maladaptive social behaviors including aggressive temperament in offspring.
- Smoking (strongly) and caffeine (weakly) reduce MAO activity and raise catecholamine levels. Hence people suffering from depression often self-medicate with these substances. Using food and herbs to slow MAO (see below) may help when quitting smoking.
- Alcohol actually increases MAO activity, but some alcoholic beverages at the time of consumption can overwhelm MAO capacity. This is why alcohol can cause an initial “antidepressant/euphoric” effect as it temporarily reduces the degradation of serotonin and dopamine. However, excessive or “binge” drinking causes a rapid build-up of chemicals, which can result in both immediate mood changes and also long-term neurological damage. Alcoholic beverages containing high levels of amines such as champagne and wine increase MAO workload to the greatest extent. To improve mood, MAOA activity may be regulated naturally with healthy foods and supplements (see below).

Food:

- Avoid simple, processed carbohydrates; riboflavin (B2)-deficient diet, iron-deficient diet.
- Foods containing naturally-occurring amines may reduce the capacity of MAO enzymes to degrade serotonin (an internally-produced amine). These include tyramine containing foods: aged cheeses; cured, smoked or processed meat or fish; fermented foods and sauces: yeast spreads (marmite), tempeh, miso, tamari; beer, wine and champagne; tofu and soy milk, fava beans and snow peas.
- Avoid excessive consumption of tryptophan rich foods for the same reason.

Slows down your MAOA gene, continued...

Supplements and Medications:

- Although tryptophan is required for serotonin production, excessive tryptophan supplementation can slow MAOA by increasing its workload. This may result in hyperactivity and sweating. Therefore, do not over supplement but use the pulse method instead.
- For those with a fast MAOA genotype that is expressing itself (or your MAOA is acting fast due to other factors such as chronic stress or low estrogen), then these supplements may be useful to calm a fast MAOA: 5-hydroxytryptophan (5-HTP), garlic extract, berberine, curcumin, quercetin, green tea, *Rhodiola rosea*.
- Many medications interact with this enzyme, especially reversible MAO inhibitors such as pseudoephedrine, ephedrine, norephedrine. Beware concurrent use of multiple medications as MAO inhibition effects are often additive. Consult your healthcare provider or pharmacist.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Speeds up your MAOA gene

Lifestyle:

- Chronic, low-level stress causes MAO enzymes to upregulate presumably as a result of the need to break down the increased amount of stress hormones being produced.
- Alcohol increases MAO activity, which reduces important neurotransmitters, and may result in both neurological and immunological deregulation. While drinking alcohol is not encouraged, if occasional alcoholic beverages are consumed then non-tyramine containing alcohols such as gin, vodka, rum, bourbon are better choices, especially if you take a MAO inhibitor.
- Low estrogen tends to raise MAOA activity. Therefore, the postpartum estrogen drop, as well as perimenopausal estrogen decline, seem to relate to upregulated MAOA levels in the brain. Fluctuations in estrogen during the menstrual cycle may contribute to mood swings through a similar relationship.
- MAOA activity tends to naturally increase throughout adolescence into adulthood.

Food: Iron rich, riboflavin (B2), vitamin C and E rich

Speeds up your MAOA gene, continued...

Supplements and Medications:

- Optimize riboflavin (B2) and iron.
- Vitamin C and vitamin E are free radical scavengers and reduce the hydrogen peroxide produced by MAO. PQQ (pyrroloquinoline quinone) and liposomal glutathione also assist with hydrogen peroxide removal.
- Lithium at low dose, together with adequate B2, is very useful to support a slow MAOA which is causing symptoms of high serotonin. Lithium activates the serotonin transporter SLC18A1 and helps to clear excess serotonin, thus reducing the workload on MAOA. Consider low dose lithium orotate 5 mg per day as required.

THE MAOB GENE

The MAOB (monoamine oxidase B) gene produces an enzyme that catalyzes the removal of an amine group from both internally-produced and externally-derived dietary and environmental amines. It is the predominant form of MAO in the brain. Riboflavin (B2) is the cofactor required for MAOB enzyme and the by-products of this reaction are hydrogen peroxide (H_2O_2) and ammonia (NH_3).

Significant amounts of glutathione are required to neutralize this hydrogen peroxide.

In the Serotonin Pathway, MAO enzymes process and detoxify the neurotransmitter serotonin. In all of these reactions, MAOA represents the major route, and MAOB the minor route. Serotonin is a neurotransmitter that helps us feel at peace, optimistic, and self-confident. However, serotonin can easily become dysregulated. Low levels of serotonin can cause anxiety, depression, cravings and insomnia. High levels of serotonin can also cause anxiety (this time associated with irritability rather than depression), as well as rapid heart rate, high blood pressure and a host of other symptoms.

MAO enzymes are located on the X chromosome. Therefore, males only inherit one allele and females have inherently higher activity as a result of two X chromosomes.

Slows down your MAOB gene

Lifestyle:

- Avoid alcohol (more than one glass), caffeine (weakly inhibits), iron deficiency anemia, smoking (both active and passive exposures).
- Short-term, acute, high stress situations reduce the activity of MAOB enzymes (as response to the "fight or flight" situation by reducing the break down of stress hormones).
- Stress sensitive females (higher basal heart rate, lower peak estrogen and progesterone) appear to have less activity.
- Males have only one copy, so inherently possess less activity.

Notable variation:

SNP: **MAOB -36A>G rs1799836 (-/-, TT)**

There is no direct research for how this variant may alter the conversion of serotonin to 5-HIAL in healthy or diseased individuals. MAOB has a much lower affinity for serotonin compared to dopamine. Studies into conditions related to serotonin metabolism like PTSD, tension headaches see no difference between C as compared to the T variant indicating likely no change in serotonin handling.

SNP: **MAOB 15106T>C rs5905512 (+/+, AA)**

This variant (AA in women, A in men) is not yet well studied in terms of its functional consequences. However, in diseased states, it may be upregulated. It is included here for investigational purposes in anticipation of future research that can better characterize its impact.

Slows down your MAOB gene, continued...

Food:

- Avoid simple, processed carbohydrates; riboflavin (B2)-deficient diet, iron-deficient diet.
- Foods containing naturally-occurring amines may reduce the capacity of MAO enzymes to degrade serotonin (an internally-produced amine). These include tyramine containing foods: aged cheeses; cured, smoked or processed meat or fish; fermented foods and sauces: yeast spreads (marmite), tempeh, miso, tamari; beer, wine and champagne; tofu and soy milk, fava beans and snow peas.
- Avoid excessive consumption of tryptophan rich foods for the same reason.

Supplements and Medications:

- Excessive tryptophan will dirty MAOB by increasing its workload and this may result in hyperactivity and sweating. Therefore, do not over supplement but use the pulse method instead. However, if your fast MAOB genotype is expressing itself (or your MAOB is acting fast due to other factors such as chronic stress or low estrogen), then these supplements may be useful to calm a fast MAOB: Garlic extract, berberine, curcumin, quercetin, EGCG from green tea, silymarin, *Glycyrrhiza spp.* (licorice), *Lamiaceae* (mint family: lavender, oregano, rosemary, sage, thyme, etc); *Rhodiola rosea*, *Scutellaria spp.* (skullcap), *Piper methysticum* (kava-kava), *Baptisia officinalis* (wild indigo), gentian, *Symphytum spp.* (comfrey), *Phellodendron amurense* (Amur corktree), *Cyamopsis psoralioides* (bakuchi seed), *Psoralea corylifolia* (babchi seed).
- A comprehensive list of herbs with MAOB inhibition effects can be found in Table 1 here.
- Many medications interact with this enzyme, especially reversible MAO inhibitors such as pseudoephedrine, ephedrine, norephedrine. Beware concurrent use of multiple medications as MAO inhibition effects are often additive. Consult your healthcare provider or pharmacist.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Speeds up your MAOB gene

Lifestyle:

- Long-term, low-level ongoing stress causes MAOB upregulation. MAOB activity also naturally increases with age.
- Estrogen tends to inhibit MAOB, therefore an age-related decline in estrogen is likely to further increase MAOB activity. Since MAOB processes serotonin in the brain and central nervous system, increased MAOB activity causes a depletion of serotonin and may exacerbate issues such as post-menopausal depression.
- Alcohol increases MAOB activity, further increasing the risk of mood swings and depression. While drinking alcohol is not encouraged, if occasional alcoholic beverages are consumed then non-tyramine containing alcohols such as gin, vodka, rum, bourbon are better choices, especially if you take a MAO inhibitor.

Food: Iron, riboflavin (B2), vitamin C and E rich

Supplements and Medications: Optimize riboflavin (B2) and iron. Vitamin C and vitamin E are free radical scavengers and reduce the hydrogen peroxide produced by MAO. PQQ (pyrroloquinoline quinone), liposomal glutathione or S-acetyl glutathione also support elimination of hydrogen peroxide.

THE ADH1B/1C GENE

The ADH1B and ADH1C (alcohol dehydrogenase 1B/1C) genes express enzymes which detoxify a wide variety of alcohol substrates: ethanol, retinol, other aliphatic alcohols, hydroxysteroids and lipid peroxidation products.

In the Serotonin Pathway, ADH1B converts 5-hydroxyindole- acetaldehyde (5-HIAL) to 5-hydroxytryptophol (5-HTOL), using the cofactors zinc and NAD+, the active form of niacin (B3).

Dirties your ADH1B/1C gene

Environment: Avoid acetaldehyde from the environment such as smog, vehicle emissions, smoking (especially secondhand exposures), cooking fumes, formaldehyde from building materials, industrial air pollution and disinfectants, drugs and perfumes; lead, mercury, dioxin compounds.

Lifestyle:

- Smoking and alcohol reduces ADH capacity to detoxify alcohol itself.
- High T4/hyperthyroidism may reduce production of ADH in the liver.
- Treat any *Candida* dysbiosis which generates endogenous acetaldehyde.
- Females tend to have lower ADH activity and ADH activity in males reduces with age.

Food: Limit fermented foods high in acetaldehyde such as yogurt, vinegar, kombucha, fish products, fermented mushrooms, miso, tempeh, pickled vegetables and kimchi. Other foods containing acetaldehyde include very ripe fruit, artificial flavors like lemon flavoring, ground and instant coffee. Many aldehydes are found in drinking water so use a filter. Avoid foods and drinks containing aspartame which are metabolized to formaldehyde.

Supplements and Medications: Avoid H2 blockers (Tagamet, Fluxid, Pepcid, Axid, Zantac). Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your ADH1B/1C gene

Environment: Employ strategies to reduce exposure to sources of acetaldehyde in the environment.

Lifestyle: Ensure sufficient bile acid production as bile acid helps to activate ADH activity.

Food: Zinc and niacin (B3) rich

Notable variation:

While no notable variation was found, we are presenting this gene's information to you because it's so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

Cleans your ADH1B/1C gene, continued...

Supplements and Medications:

- Choose zinc, niacin (B3) rich sources. Thiamine (B1) is also especially important as acetaldehyde damages enzymes which are B1 dependent.
- Consider resveratrol with vitamin C (especially when consuming alcohol).
- Some herbs have been shown in mice to slow down the biotransformation of alcohol into the more toxic acetaldehyde. These herbs include *Acanthopanax sessiliflorus, Ixeris dentata, Glycyrrhiza uralensis* (Chinese licorice), *Hovenia dulcis* (Japanese raisin tree), *Liriope platyphylla* (lilyturf), *Lycium chinense* (goji berry), *Pueraria thunbergiana* (kudzu).

THE ALDH2 GENE

The ALDH2 (aldehyde dehydrogenase 2 family member) gene expresses an enzyme which converts aldehydes to carboxylic acids.

In the Serotonin Pathway, ALDH2 converts 5-hydroxyindole- acetaldehyde (5-HIAL) to the final product 5-hydroxyindoleacetic acid (5-HIAA), which is excreted in the urine. This reaction uses niacin (B3) as a cofactor.

ALDH2 also performs the vital role of neutralizing internally-produced lipid peroxidation products formed due to oxidative stress.

Many commonly found environmental chemicals put additional strain on this enzyme.

Dirties your ALDH2 gene

Environment: Avoid aldehydes from the environment such as vehicle emissions, smoking (especially secondhand exposures), cooking fumes, formaldehyde from building materials, disinfectants, drugs, perfumes, fungicides and pesticides, carbon tetrachloride (dry cleaning), hydrogen sulfide and many other environmental chemicals. Also minimize oxidative stress to decrease aldehydes created internally by reactive oxygen species.

Lifestyle: Limit alcohol, smoking, insulin resistance, oxidized LDL, high kynurenine which can all inhibit ALDH2. Work with your healthcare provider to identify *Candida* dysbiosis which generates endogenous acetaldehyde.

Food: Limit oxidized omega-6 fatty acids (from old or processed oils), known allergens, foods high in acetaldehyde such as fish products, canned vegetables, fermented foods: yogurt, vinegar, kombucha, fermented mushrooms, tempeh, miso, pickled vegetables and kimchi. Other foods containing acetaldehyde include very ripe fruit, artificial flavors like lemon flavoring, ground and instant coffee. Many aldehydes are found in drinking water so use a filter. Avoid foods and drinks containing aspartame which are metabolized to formaldehyde.

Supplements and Medications: Acetaminophen (Tylenol), aspirin

Cleans your ALDH2 gene

Environment: Employ strategies to reduce exposure to sources of acetaldehyde and other environmental chemicals.

Food: Choose vitamin B1, B3, C zinc, magnesium rich sources; especially when consuming alcohol. Opt for a diet rich in vegetables from the brassica family, broccoli sprouts.

Notable variation:

SNP: **ALDH2 699T>C rs737280 (+/+, CC)**

This CC variant may decrease enzyme activity and makes exposures to pesticides more risky. Due to lack of research in other ethnicities, these results may be applicable only to those of European descent.

Cleans your ALDH2 gene, continued...

Supplements and Medications:

- Thiamine (B1) is especially important as acetaldehyde damages enzymes which are B1 dependent. Consider zinc, niacin (B3), sulforaphane, resveratrol with vitamin C (especially when consuming alcohol).
- Some herbs have been shown in mice to speed up the biotransformation of acetaldehyde into less toxic end products. These herbs include *Lycium chinense* (goji berry), *Acanthopanax sessiliflorus*, *Ixeris dentata*, *Polypori umbellati* (zhu ling).

THE CYP1A2 GENE

The CYP1A2 (cytochrome P450 monooxygenase 1A2) gene expresses an enzyme which is involved in degrading various compounds made in the body such as fatty acids, steroid hormones, vitamins, melatonin and cholesterol. It also detoxifies ingested compounds such as caffeine, aflatoxin B1 and many medications.

CYP1A2 requires oxygen and heme as necessary cofactors.

The issue of speed/rate of degradation of compounds by CYP1A2 is somewhat moot, as some end products are less toxic while others are more toxic.

The overall transformation rate of any compound by this enzyme also varies on any given day depending on the exposures encountered that impact the enzyme: dietary choices, environmental contaminants, medications.

Slows down your CYP1A2 gene

Lifestyle:

- Alcohol; coumarins found in perfumes, shampoos, lotions, body care products which are significantly absorbed through the skin all slow this enzyme.
- Evaluate heme deficiency. Heme is a cofactor for CYP1A2. However, many parasites and gram negative bacteria need the iron-containing cofactor, heme, to reproduce and cause infection. Parasites and bacterial pathogens must synthesize their own heme or acquire heme from the host. Thus, untreated chronic parasites and bacterial infections may create a heme deficiency.
- Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.
- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage due to low heme.

Notable variation:

SNP: **CYP1A2 -163C>A rs762551 (+/-, AC)**
Smoking and non-smoking CA individuals metabolized caffeine at the same rate as non-smoking AA and CC individuals. Thus, having at least one C variant allele appears to diminish the inducibility/speeding up of the CYP1A2 by polyaromatic hydrocarbons (PAH) such as smoke exposures and high coffee consumption.

Some research has specifically analyzed melatonin metabolism in regard to genotype and smoking, and surprisingly saw no correlation between smoking, genotype and melatonin metabolism although the study was small in size.

CYP1A2 is a phase 1 liver enzyme that is responsible for metabolizing a vast array of chemical compounds found in our food, environment and medications. Some of these, like smoke or polyaromatic hydrocarbons (PAH) in our diet, can upregulate the enzyme, while other compounds downregulate the enzyme. Thus, the activity of the enzyme is fluctuating constantly to respond to these many inputs and demands in addition to the influence of SNPs that control the expression of CYP1A2 (other CYP1A2 and AHR SNPs).

This CA genotype is typically called by some genetic reports "intermediate metabolizers" of caffeine, but this is likely a vastly over-simplified and misleading representation, as the effect of coffee on sleep and mood depends on many genes: COMT, AHR, ADORA2A, DRD2, as well as diet and lifestyle. Since the C variant seems to diminish enzyme upregulation from polyaromatic hydrocarbons, habitual heavy coffee drinkers or smokers do not necessarily have an upregulated CYP1A2 in response to PAHs, especially if they also simultaneously eat foods or take medications known to inhibit CYP1A2.

Slows down your CYP1A2 gene, continued...

Food:

- A diet rich in vegetables from the umbel (carrot) family: carrots, celery, celeriac, cilantro, fennel, parsley, parsnips; as well as seeds from this family commonly used as spices: asafoetida, caraway, coriander, cumin, dill, fennel, curry powder all slow this enzyme.
- Other inhibitors include grapefruit and its juice; naturally occurring coumarin rich spices; foods such as Cassia cinnamon, Mexican vanilla, tonka beans, strawberries, bilberries, cherries, apricots, green tea, honey.
- Meat cooked using methods that employ lower, indirect heat such as braising or stewing can decrease polyaromatic hydrocarbon (PAH) formation. Polyaromatic hydrocarbons from chargrilling meat may also be reduced by marinating meats for 4 hours prior to grilling in beer, vinegar or tea (both green or black) based sauces including lemon, onions, garlic, or alternatively: spraying meat with culinary vinegar prior to grilling. Polyaromatic hydrocarbon formation was decreased by almost 80% using white wine vinegar, 66% by red wine and cider vinegar, and 55% by raspberry vinegar. Use the extractor hood while cooking along with high smoke point oils such as avocado or ghee.

Supplements and Medications: Caffeine alone (not coffee); herbs high in coumarins such as *Artemisia spp.* (wormwood), *Verbascum thapsus* (mullein), *Melilotis spp.* (sweet clover), *Angelica spp.* (dong quai), *Ferula communis, Glycyrrhiza spp.* (licorice), *Mentha spp.* (peppermint and spearmint) all have potential to inhibit. H2 blockers (Tagamet, Fluxid, Pepcid, Axid, Zantac); antibiotics, estrogens and oral contraceptives containing estrogens can slow CYP1A2. Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Speeds up your CYP1A2 gene

Environment: Smoke from any source: cigarettes, marijuana, incense, woodsmoke, diesel exhaust, smog, cooking fumes.

Food:

- Opt for a diet rich in vegetables from the brassica family.
- Avoid foods high in polyaromatic hydrocarbons: meat, fish, shellfish and poultry especially if smoked; food products of any type originating from polluted environments (e.g., produce grown near highways or downwind from air pollution sources) or cooked over woodfire; deep-fried foods, coffee, baked goods: especially bread and pizza from wood-fired ovens. All these food products can speed up and overtax CYP1A2.
- Heavy coffee use (3 or more cups/day) will increase activity of CYP1A2 due to the polyaromatic hydrocarbon content of roasted coffee beans.

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

THE CYP1B1 GENE

The CYP1B1 (cytochrome P450 monooxygenase 1B1) gene expresses an enzyme which, using oxygen and heme as cofactors, degrades melatonin in tissues other than the liver such as the retina and the colon.

CYP1B1 also plays an important role throughout the body in the first phase of detoxifying compounds such as polycyclic aromatic hydrocarbons (PAH), dietary plant flavonoids, genotoxic catechol estrogens, and converting retinol (a vitamin A compound) to retinal.

The rate of degradation by CYP1B1 is a somewhat moot issue, as some end products are less toxic while others are more toxic.

The overall transformation rate of any compound by this enzyme also varies on any given day depending on the exposures encountered that impact the enzyme: dietary choices, environmental contaminants, medications, etc.

Slows down your CYP1B1 gene

Environment: Use an extractor hood while cooking and high-smoke point oils such as ghee or avocado oil.

Lifestyle:

- Many parasites and gram negative bacteria need the iron-containing cofactor, heme, to reproduce and cause infection. Parasites and bacterial pathogens must synthesize their own heme or acquire heme from the host. Thus, untreated chronic parasites and bacterial infections may create a heme deficiency. Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.
- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage as heme is the required cofactor for this enzyme.

Food: Choose meat cooking methods that employ lower, indirect heat such as braising or stewing which decrease polyaromatic hydrocarbon (PAH) formation. Polyaromatic hydrocarbons (PAH) from chargrilling meat may also be reduced by marinating meats for 4 hours prior to grilling in beer, vinegar or tea (both green or black) based sauces including lemon, onions, garlic, or alternatively: spraying meat with culinary vinegar prior to grilling. Polyaromatic hydrocarbon formation was decreased by almost 80% using white wine vinegar, 66% by red wine and cider vinegar, and 55% by raspberry vinegar. Use high smoke point oils such as ghee or avocado oil.

Notable variation:

SNP: **CYP1B1 CYP1B1*4 rs1800440 (-/-, TT)**

Considered wild type or ancestral allele, this TT variant has 3x the expression level and longer enzymatic half-life than the mutated variant in vitro. This can actually be a drawback as catechol estrogens and environmental chemicals are bio-activated by this enzyme at a rate faster than the downstream water solubilizing enzymes can handle. Little is known about how this CYP1B1 variant affects melatonin metabolism.

Slows down your CYP1B1 gene, continued...

Supplements and Medications:

- Diindolylmethane (DIM), quercetin, kaempferol, flaxseed, resveratrol, *Humulus lupulus* (hops), *Trifolium praetense* (red clover) all have potential to slow CYP1B1.
- In the end, it is impossible to predict with pinpoint accuracy how an individual will react to a given dose of substrate metabolized by CYP1B1, as its activity is dynamic and reflects changing diet and environmental conditions. If melatonin for sleep at bedtime results in daytime grogginess, consider decreasing the amount taken as there may be slower metabolism of melatonin due to this genetic variant as well as interaction with other metabolizing genes or diet. Conversely, melatonin for sleep at bedtime may not result in improved sleepiness. If this describes you, consider increasing the amount taken or use a time release form as there may be faster metabolism of melatonin due to this genetic variant as well as interaction with other metabolizing genes or diet.
- Special notes for melatonin dosing: One study looked at a very small number of autistic children who stopped responding to bedtime dosing (ranging from 2.5 to 10 mg) of melatonin after initial improvement in sleep. The children were determined to be slow melatonin metabolizers as evidenced by high plasma melatonin levels during midday when levels should have been low. Reducing dose to 0.1 mg restored efficacy of bedtime melatonin for sleep. This study did not examine CYP1B1 genotype but did look at CYP1A2 status and most were what is considered the "fast" metabolizer of caffeine genotype. In short: genotype is not always predictive of response in an individual.

Speeds up your CYP1B1 gene

Environment: Smoke from any source such as incense, woodsmoke, air pollution, vehicle exhaust, cooking especially with low smoke point oils

Lifestyle: Smoke from any source: cigarettes, marijuana, secondhand exposures will induce this enzyme.

Food:

- Avoid high-temperature cooking methods that generate polyaromatic hydrocarbons (PAH). These include grilling, charring, barbecuing and deep-frying. Avoid cured/smoked deli foods, burnt toast and high-temperature roasted items such as coffee. Avoid food products of any type originating from polluted environments (e.g., produce grown near highways or downwind from air pollution sources).
- Normal function requires biotin, vitamin A, beta carotene and iron-rich foods. Avoid the standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium, oxidized inflammatory fats, and low in fiber and good quality protein.

Supplements and Medications: Consider biotin, vitamin A or beta carotene and iron.

THE UGT1A GENE

The UGT1A6 (UDP-glucuronosyltransferase family 1 member A6) gene expresses an enzyme in the phase II liver glucuronidation pathway which is important in the elimination of potentially harmful xenobiotics and endogenous compounds such as steroids, bilirubin, hormones, and drugs (especially aspirin and acetaminophen).

In the Serotonin Pathway, UGT is the major route for the excretion of 5-hydroxytryptophol (5-HTOL), which is a metabolite of serotonin.

Dirties your UGT1A gene

Environment: Many environmental chemicals are detoxified by the UGT1A6 enzyme and can have long-term inhibitory effects on the glucuronidation capacity of the liver. These include:

- Persistent organochlorine pollutants such as PCB, DDT, bisphenol A (BPA), plastics, compounds in some antibacterial soaps and dioxin-like compounds.
- Xenobiotic compounds (such as 1-naphthol, 4-nitrophenol, 4-methylumbelliferone) found in fabric dyes, hair dyes, skin lightening products and certain pesticides and herbicides.

Lifestyle:

- UGT1A6 activity naturally declines with advancing age and females naturally have lower expression than males.
- Inflammation and infections, especially LPS from bacterial infections and leaky gut, accelerate this decline.

Food:

- Limit synthetic food dyes (such as halogenated xanthene food dyes, phloxine, erythrosine, and rose bengal).
- Avoid high-temperature cooking methods that generate polyaromatic hydrocarbons (PAH) in foods through burning and smoke such as grilling, charring, barbecuing and deep-frying.
- Avoid cured/smoked deli foods, bread and pizza from wood-fired ovens, burnt toast, high-temperature roasted items.
- Avoid any type of food products originating from polluted environments (e.g., produce grown near highways or downwind from air pollution sources).

Notable variation:

A less common UGT1A6 Haplotype

The haplotype combination you possess falls somewhere between the functional effect of two copies of UGT1A6*2 compared with 2 copies of UGT1A6*1 (wild type). The speed of turnover depends on the substrate. With regard to serotonin, 5-hydroxytryptophol, 4-nitrophenol, and acetaminophen, your haplotype is likely faster than 2 copies of UGT1A6*1 (wild type), but slower than two copies of UGT1A6*2.

It appears that your haplotype, having one copy of UGT1A6*2 or the other less common variants, also exhibited 15-35% slower glucuronidation of common medications like aspirin and beta blockers compared to wild type. In general, males have higher activity than females.

Overall, these variants were predicted to account for only 15-20% of the observed 1300% variability in glucuronidation of UGT1A6 substrates by human liver microsomes suggesting that environmental influence is huge.

Gene	rsID	Alias	Variant Allele	Call
UGT1A6	rs6759892	Ser7Ala	G	TG
UGT1A6	rs2070959	Thr181Ala	G	AA
UGT1A6	rs1105879	Arg184Ser	C	AA

Dirties your UGT1A gene, continued...

Supplements and Medications: Many natural compounds found in fruit, vegetables and herbs are processed by the UGT1A6 enzyme. Thus, the theory is that these compounds may 'use up' the capacity of the enzyme, leaving less capacity for detoxification of toxic environmental chemicals and medications. However, these natural, botanical compounds have many health-promoting properties and are an important part of a healthy diet. Additionally, they have antioxidant and liver-protective properties which help to reduce the damage caused by environmental chemicals. Rather than avoiding these natural, health-promoting compounds, concentrate on reducing your exposure to damaging environmental chemicals.

When taking medications, consult your healthcare provider. Certain drugs that are detoxified by the UGT1A6 enzyme may have drug interactions with natural compounds that are also processed by this glucuronidation pathway. Many botanical compounds have actually been shown to enhance the bioavailability of certain drugs by inhibiting the activity of UGT enzymes. As a result, lower doses of the drugs may be required to achieve the same therapeutic effect. However, it is crucial to closely monitor this interaction to ensure optimal efficacy and safety. This is especially important for people with variants that already slow the UGT1A6 enzyme activity.

Herbs with potential for drug interactions due to inhibition of UGT1A6 include: Silybum marianum (milk thistle), Astragali radix (astragalus or “Huang Qi” in Chinese), Hypericum perforatum (St. John’s wort), Serenoa repens (saw palmetto) and cranberry. These herbs only need to be considered if you are taking medications that are detoxified via the glucuronidation process.

Herbs high in coumarins have many medicinal properties but may also have drug interactions with certain medications. Consult your healthcare provider. Such herbs include: Artemisia spp. (wormwood), Verbascum thapsus (mullein), Melilotis (sweet clover), Angelica (dong quai), Ferula communis, Mentha (peppermint and spearmint)

Many medications interact with this enzyme, especially non-steroidal anti-inflammatory drugs (NSAIDs), aspirin and acetaminophen (Tylenol). Consult your healthcare provider or pharmacist.

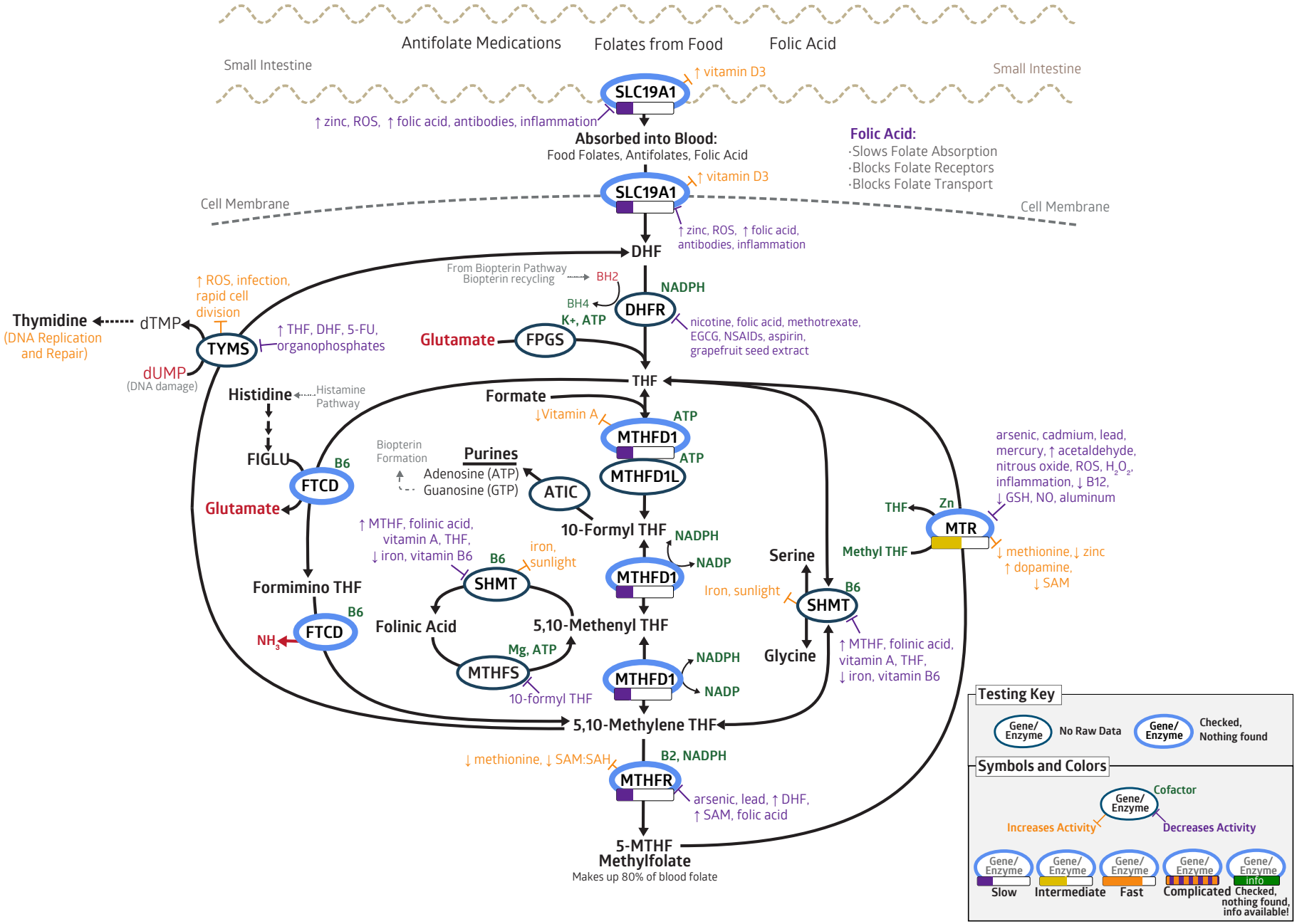
Cleans your UGT1A gene

Food:

- Consume a wide variety of colourful fruits and vegetables especially cruciferous vegetables containing sulforaphane and quercetin such as broccoli, kale, onion and garlic.
- Choose teas such as green tea, rooibos, honeybush or dandelion.
- Choose meat cooking methods that employ lower, indirect heat such as braising or stewing which decrease polyaromatic hydrocarbon formation (PAH). PAH from chargrilling meat may be reduced by marinating meats for 4 hours prior to grilling.
- When roasting, add rosemary and lemon juice. These may increase UGT1A6 activity (conflicting data). They also help to improve the detoxification of compounds generated during the roasting process.
- Coffee appears to up-regulate glucuronidation. Choose high quality, preferably organic coffee, without milk or sugar. Do not over-consume as coffee is a stimulant. Additionally, be aware of medications that may be detoxified more quickly with coffee.

Supplements and Medications:

- Consider calcium-D-glucarate.
- Certain compounds such as quercetin, curcumin, glycyrrhiza (licorice) and piperine (black pepper) may technically slow UGT1A6 enzyme function but have also been shown to increase its expression (the amount of the enzyme present). Thus they tend to have an overall supportive effect on glucuronidation.
- Antioxidants such as astaxanthin, vitamin C, vitamin E and glutathione are useful for reducing oxidative stress caused by environmental chemicals.


Antifolate Medications
Folates from Food
Folic Acid
Small Intestine
Small Intestine
↑ vitamin D3
SLC19A1
↑ zinc, ROS, ↑ folic acid, antibodies, inflammation
Absorbed into Blood:
Food Folates, Antifolates, Folic Acid
Folic Acid:
·Slows Folate Absorption
·Blocks Folate Receptors
·Blocks Folate Transport
↑ vitamin D3
SLC19A1
Cell Membrane
Cell Membrane
↑ zinc, ROS, ↑ folic acid, antibodies, inflammation
DHF
From Biopterin Pathway
Biopterin recycling
BH2
BH4
NADPH
DHFR
K+, ATP
nicotine, folic acid, methotrexate, EGCG, NSAIDs, aspirin, grapefruit seed extract
↑ ROS, infection, rapid cell division
Thymidine
(DNA Replication and Repair)
dTMP
TYMS
↑ THF, DHF, 5-FU, organophosphates
dUMP
(DNA damage)
Glutamate
FPGS
THF
Histidine
Histamine Pathway
Formate
↓Vitamin A
ATP
MTHFD1
ATP
MTHFD1L
FIGLU
B6
FTCD
Glutamate
Biopterin Formation
Purines
Adenosine (ATP)
Guanosine (GTP)
ATIC
10-Formyl THF
NADPH
NADP
MTHFD1
↑ MTHF, folinic acid, vitamin A, THF, ↓ iron, vitamin B6
B6
iron, sunlight
SHMT
Formimino THF
B6
FTCD
NH3
Folinic Acid
5,10-Methenyl THF
Mg, ATP
MTHFS
10-formyl THF
NADPH
NADP
MTHFD1
5,10-Methylene THF
Serine
Iron, sunlight
B6
SHMT
Glycine
↑ MTHF, folinic acid, vitamin A, THF, ↓ iron, vitamin B6
THF
Zn
MTR
Methyl THF
arsenic, cadmium, lead, mercury, ↑ acetaldehyde, nitrous oxide, ROS, H2O2, inflammation, ↓ B12, ↓ GSH, NO, aluminum
↓ methionine, ↓ zinc
↑ dopamine,
↓ SAM
↓ methionine, ↓ SAM:SAH
B2, NADPH
MTHFR
arsenic, lead, ↑ DHF, ↑ SAM, folic acid
5-MTHF
Methylfolate
Makes up 80% of blood folate
Testing Key
Gene/ Enzyme
No Raw Data
Gene/ Enzyme
Checked, Nothing found
Symbols and Colors
Cofactor
Gene/ Enzyme
Increases Activity
Decreases Activity
Gene/ Enzyme
Slow
Gene/ Enzyme
Intermediate
Gene/ Enzyme
Fast
Gene/ Enzyme
Complicated
Gene/ Enzyme
info
Checked, nothing found, info available!

THE SLC19A1 GENE

The SLC19A1 (solute carrier family 19) gene expresses a transport protein which carries folate across the intestinal lining and also into and out of cells.

There are different folate transporters (SLC19A1 is one of them). Each has a different affinity for the three different types of folates (naturally occurring folate, synthetic folic acid and antifolate medications). SLC19A1 has a higher affinity for natural folate than synthetic folic acid.

Dirties your SLC19A1 gene

Environment: Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections.

Lifestyle: Avoid alcohol, inflammation, infection, oxidative stress. Also limit excessive exercise which is an overlooked factor in increased oxidative stress.

Food: Elevated blood sugar, prolonged high fat diet such as a ketogenic diet (likely due to low folate intake), foods or beverages enriched with synthetic folic acid can all interfere with SLC19A1. Folate receptor auto-antibodies may also contribute to folate transport issues. Folate receptor auto-antibodies appear to be caused by high homocysteine as well as allergic response to dairy of all types including cow, goat and camel.

Supplements and Medications: Limit antacids, proton pump inhibitors (Prilosec, Prevacid, Nexium). Synthetic folic acid should also be avoided as it reduces the amount of folate transport proteins. If one has a high amount of synthetic folic acid in the blood compared to natural folates (folinic acid and methylfolate), then these natural folates may not be transported well. In addition, many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your SLC19A1 gene

Lifestyle: Optimize stomach acid production.

Food: Focus on vitamin D and natural folate rich foods. Emphasize whole, minimally processed foods, as processed foods often contain synthetic folic acid; read the nutrition label. Consider IgE and IgG food allergy tests along with folate receptor antibody tests.

Supplements and Medications: Optimize vitamin D, natural folates (folinic acid and methylfolate) levels. Studies indicate that high levels of supplemental zinc may compete with the absorption of folate. In some situations, a higher intake of zinc may be useful while sustained high levels may have negative consequences. Always strive to optimize levels of zinc and other nutrients with your health professional.

Notable variation:

SNP: **SLC19A1 G80A rs1051266 (+/-, TC)**

This TC variant appears to have little to no impact on folate transport compared to wild type CC. However, as a precaution, carriers of this variant should avoid synthetic forms of folate, found in processed foods and many supplements.

Use nutrients to support optimization of homocysteine levels (6 umol/L - 8 umol/L) and repair a leaky gut which can reduce antibodies to foods. Fewer antibodies to food antigens can reduce the risk of cross reactivity that produces folate receptor auto-antibodies. The absence of these folate auto-antibodies enhances folate transport. Avoid synthetic folic acid. Synthetic folic acid is contraindicated in cerebral folate deficiency.

THE MTHFD1 GENE

The MTHFD1 (methylenetetrahydrofolate dehydrogenase) gene expresses an enzyme which conducts three separate enzyme activities along the path of converting tetrahydrofolate (THF) to methylfolate (5-MTHF) using NADPH and ATP as cofactors. NADPH is niacin (B3) dependent.

MTHFD1 regulates the formation of many types of folate, and all of the enzyme activities of MTHFD1 are reversible and flow in the direction-dependent upon the body's various folate requirements at any given time.

If the MTHFD1 enzyme is functioning more slowly, potentially less folinic acid and less methylfolate will be produced. Serum folates may then appear to be fine yet the reduced, more active forms of folate may be deficient. When less folate is available for the methylation cycle, choline deficiency may result. This occurs because during folate deficiency, choline steps in to help produce phosphatidylcholine and betaine.

Dirties your MTHFD1 gene

Environment: Living in sunny areas leads to increased folate demand to repair sun-damaged skin. Naturally darker skin can help, but does not reduce folate demand entirely.

Lifestyle: Pregnant or breastfeeding women use more folate and choline. 90% of women are choline deficient and if they are low in folate as well, there are going to be complications.

Food: Folate deficient diets, high fat diets, high simple carbohydrate diets and high calorie density diets may increase this gene's workload as these diets are strongly associated with fatty liver and gallstones. A choline deficient diet is also detrimental as choline is an important nutrient required for the production of phosphatidylcholine (important for healthy cell membranes) and betaine (important for homocysteine recycling). People with MTHFD1 variants are more likely than non-variant carriers to develop signs of choline deficiency on a low-choline diet. Vegans and vegetarians are more susceptible to choline deficiency as well.

Cleans your MTHFD1 gene

Environment: Protect skin from strongest sun rays of the day (10 a.m. to 4 p.m.) by using zinc oxide, hats and sun-protective clothing.

Food: Folate (B9), choline, betaine, glycine, niacin (B3) and vitamin A rich

Notable variation:

SNP: **MTHFD1 G1958A rs2236225 (+/-, AG)**

This GA variant decreases the metabolic activity of MTHFD1 within mice cells by 25% on average. The enzyme loses stability as body temperature rises so its function becomes more compromised during fevers. The activity and stability of the enzyme can be improved by sufficient folate (B9). This variant is especially worrisome for pregnant or lactating women as choline demand increases.

Cleans your MTHFD1 gene, continued...

Supplements and Medications: Folinic acid (note: not folic acid) is shown to support those with MTHFD1 insufficiency. Consider also betaine, choline bitartrate and phosphatidylcholine as choline and folate have an inverse relationship. This especially if low functioning PEMT (present) or CHDH (unknown).

If one is deficient in choline, more folate is used. If one is deficient in folate, more choline is used. Thus, supporting with folinic acid, betaine, choline bitartrate and/or phosphatidylcholine are excellent considerations.

Choose non-GMO soy or sunflower derived phosphatidylcholine. Consider glycine and serine as well. Additionally, more THF substrate may be provided by supporting the MTR gene with L-5-MTHF, methylcobalamin or hydroxocobalamin. Consider more folinic acid during exposure to summer sun, especially while pregnant or breastfeeding.

THE MTHFR GENE

The MTHFR (methylenetetrahydrofolate reductase) gene expresses an enzyme which produces the body's primary form of folate called 5-MTHF (aka 5-methyl THF, L-5-MTHF, methylfolate), which represents over 80% of the body's folate. In the process, the MTHFR enzyme uses FAD, a form of riboflavin (B2), as a cofactor.

5-MTHF is utilized in the production of S-adenosylmethionine (SAM), which subsequently regulates around 200 processes including DNA methylation, neurotransmitter and phospholipids production. Since the MTHFR gene is the rate-limiting step in the generation of 5-MTHF, it is subsequently also the rate-limiting enzyme in the whole process of SAM production.

The MTHFR gene connects the Folate Pathway, via 5-MTHF, with the SAM cycle via the MTR gene. This is why a slow MTHFR may increase homocysteine levels.

Dirties your MTHFR gene

Environment: Avoid lead and arsenic. Living in sunny areas leads to increased folate demand to repair sun-damaged skin. Naturally dark skin can reduce demand, but not entirely.

Lifestyle: Hyper and hypothyroidism, insulin resistance

Food: Foods or beverages enriched with synthetic folic acid

Supplements and Medications: Avoid synthetic folic acid, aspirin, other salicylates (NSAIDs). Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your MTHFR gene

Environment: Protect skin from strongest sun rays of the day (10 a.m. to 4 p.m.) by using zinc oxide, hats and sun protective clothing.

Food: Choose riboflavin (B2) rich, choline and betaine rich, natural folate rich, polyphenol rich, low sugar. See "Your Clean Genes Recipes" in the *Dirty Genes* book.

Notable variation:

SNP: **MTHFR C677T rs1801133 (+/+, AA)**

This AA variant decreases binding of the cofactor, riboflavin (B2), which decreases MTHFR enzyme activity by 55 to 75% less than wild type. The enzyme loses stability as body temperature rises, so its function becomes compromised during fevers. The activity and stability of the enzyme improves by consuming sufficient folate (B9) and riboflavin (B2).

Cleans your MTHFR gene, continued...

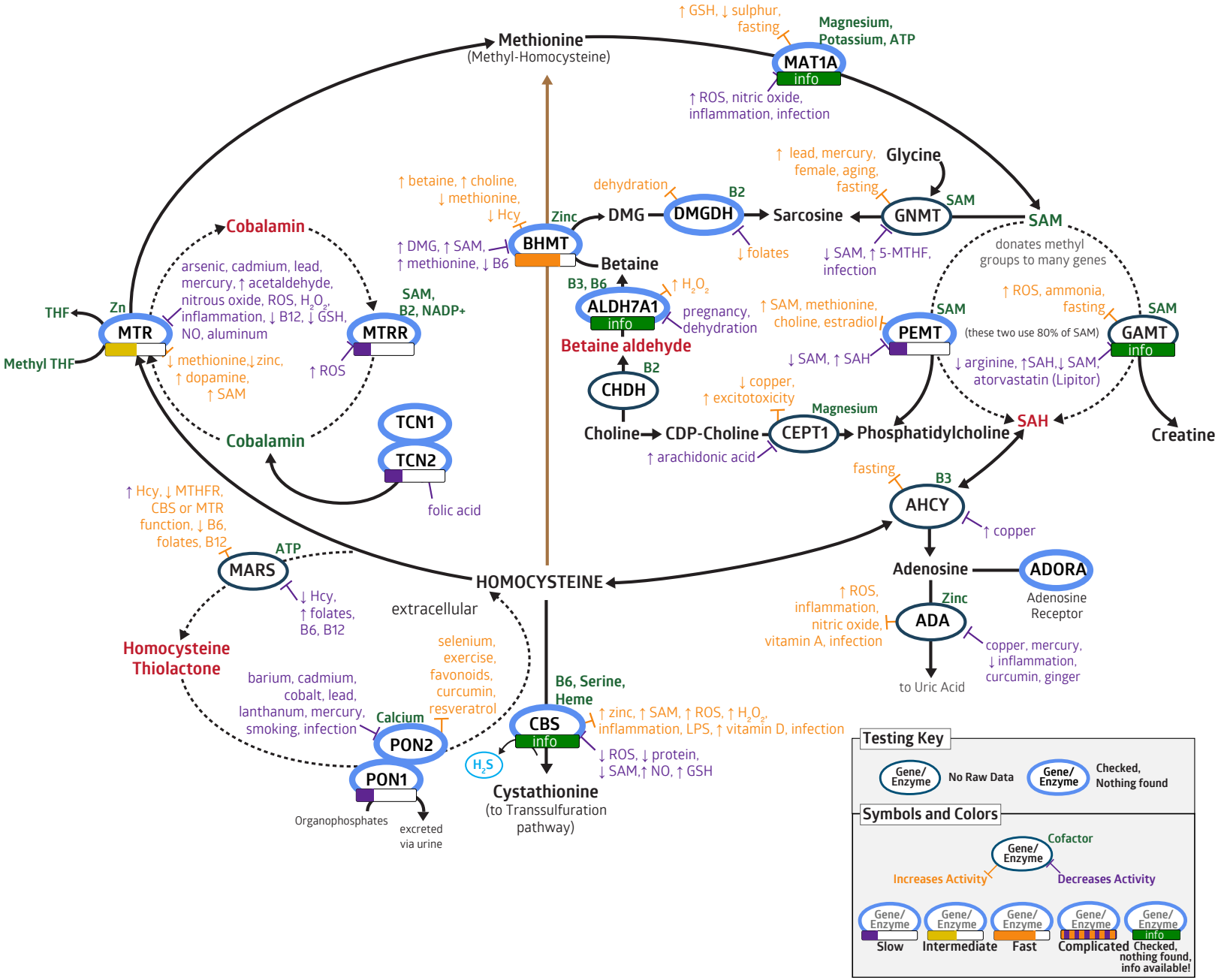
Supplements and Medications: The MTHFR enzyme produces methylfolate (5-MTHF). Thus, supplementing with L-5-MTHF may be useful. Be careful, however, as this is a very powerful type of folate. Often it is over-prescribed and leads to many side effects. If using it, consider lower amounts such as 400 mcg to 1,000 mcg of L-5-MTHF.

A way to support MTHFR with fewer side effects is to optimize the cofactor riboflavin (B2), although sufficient B2 cannot help if one is folate deficient.

Another way to support this gene is by indirectly supporting methylation by using supplements which conserve SAM. The body's production of both creatine and phosphatidylcholine use up nearly 80% of SAM; so by supplementing with them, one conserves SAM and generates less homocysteine. Choose non-GMO soy or sunflower derived phosphatidylcholine. Consider choline, betaine, omega-3: alpha-linolenic acid (ALA) and docosahexaenoic acid (DHA) fatty acids. Vitamin C showed ability to decrease hypermethylation of MTHFR in a positive way. Consider more folinic acid, L-5-MTHF or choline, whichever is well tolerated, during exposure to summer sun especially while pregnant or breastfeeding.

THE MTR GENE

The complete discussion of this gene is under SAM.


Methionine
(Methyl-Homocysteine)
↑ GSH, ↓ sulphur, fasting
Magnesium, Potassium, ATP
MAT1A
info
↑ ROS, nitric oxide, inflammation, infection
SAM
donates methyl groups to many genes
↑ lead, mercury, female, aging, fasting
Glycine
GNMT
↓ SAM, ↑ 5-MTHF, infection
dehydration
B2
DMGDH
DMG
Sarcosine
↓ folates
↑ betaine, ↑ choline, ↓ methionine, ↓ Hcy
Zinc
BHMT
↑ DMG, ↑ SAM, ↑ methionine, ↓ B6
Betaine
B3, B6
ALDH7A1
info
↑ H_2O_2
pregnancy, dehydration
Betaine aldehyde
B2
CHDH
Choline
↑ SAM, methionine, choline, estradiol
PEMT
SAM
(these two use 80% of SAM)
↓ SAM, ↑ SAH
↓ copper, ↑ excitotoxicity
Magnesium
CDP-Choline
CEPT1
Phosphatidylcholine
↑ arachidonic acid
SAH
↑ ROS, ammonia, fasting
GAMT
info
↓ arginine, ↑SAH,↓ SAM, atorvastatin (Lipitor)
Creatine
Cobalamin
arsenic, cadmium, lead, mercury, ↑ acetaldehyde, nitrous oxide, ROS, H_2O_2, inflammation, ↓ B12, ↓ GSH, NO, aluminum
THF
Zn
MTR
Methyl THF
↓ methionine,↓ zinc, ↑ dopamine, ↑ SAM
SAM, B2, NADP+
MTRR
↑ ROS
Cobalamin
TCN1
TCN2
folic acid
↑ Hcy, ↓ MTHFR, CBS or MTR function, ↓ B6, folates, B12
ATP
MARS
↓ Hcy, ↑ folates, B6, B12
HOMOCYSTEINE
extracellular
fasting
B3
AHCY
↑ copper
Adenosine
ADORA
Adenosine Receptor
↑ ROS, inflammation, nitric oxide, vitamin A, infection
Zinc
ADA
copper, mercury, ↓ inflammation, curcumin, ginger
to Uric Acid
Homocysteine Thiolactone
barium, cadmium, cobalt, lead, lanthanum, mercury, smoking, infection
selenium, exercise, favonoids, curcumin, resveratrol
Calcium
PON2
PON1
Organophosphates
excreted via urine
B6, Serine, Heme
CBS
info
↑ zinc, ↑ SAM, ↑ ROS, ↑ H_2O_2, inflammation, LPS, ↑ vitamin D, infection
↓ ROS, ↓ protein, ↓ SAM,↑ NO, ↑ GSH
H_2S
Cystathionine
(to Transsulfuration pathway)
Testing Key
Gene/ Enzyme
No Raw Data
Checked, Nothing found
Symbols and Colors
Cofactor
Increases Activity
Decreases Activity
Slow
Intermediate
Fast
Complicated
Checked, nothing found, info available!

THE MTR GENE

The MTR (methionine synthase) gene expresses a four-domain enzyme which regenerates homocysteine back to methionine, a process that ultimately generates the body's master methyl donor: S-adenosylmethionine (SAM).

MTR is a very complex and sensitive enzyme. It requires vitamin B12 and zinc as cofactors, and has to coordinate a complex interaction with the MTHFR gene (using L-5-MTHF to remethylate homocysteine back to methionine) and the MTRR gene complex (using SAM to remethylate cobalamin back to methylcobalamin). It's no wonder that high homocysteine is common!

MTR is a redox sensing gene meaning it slows down in the presence of oxidative stress. Thus, MTR is a decision-making point:

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.

Once glutathione levels are restored, oxidative stress goes down and the MTR gene can function again, recycling homocysteine back into SAM.

If the MTR substrate levels of homocysteine are too low (<5 umol/L adult), then the methylation cycle may not work sufficiently.

Dirties your MTR gene

Environment: Identify heavy metal exposures including mercury, copper, lanthanum, lead, cadmium, barium; avoid inhaled nitrous oxide aka laughing gas (dental procedures, pre-op and maternity wards); acetaldehyde (rule out *Candida* dysbiosis), oxidative stress, inflammation, chlorine, formaldehyde. It is also important to avoid factors which slow MTHFR and MTRR.

Lifestyle: Identify and treat hyper or hypothyroidism, insulin resistance. Limit alcohol, bathing in chlorinated water or frequent use of swimming pools or hot tubs. Overtraining causes significant inflammation. It is also important to avoid factors which slow MTHFR and MTRR.

Notable variation:

SNP: **MTR A2756G rs1805087 (+/-, AG)**

The functional effect of this AG variant is controversial. Older in vivo studies indicate downregulation while newer studies in humans appear to show upregulation compared to wild type AA.

This variant is a good example of a "trade-off" SNP where the minor allele, as well as wild type or ancestral allele, can be found to be epidemiologically risky or beneficial depending on environmental/epigenetic factors, degree of DNA methylation and baseline metabolic conditions in an individual.

Dirties your MTR gene, continued...

Food:

- Insufficient protein in the diet, especially if homocysteine levels are < 5 umol/L in children and adults, can slow MTR.
- Rancid cooking oils, cooking on high heat or chargrilled foods may hinder MTR due to increased demand for glutathione and thus less glutathione available for neutralizing hydrogen peroxide.
- Farmed fish can be high in heavy metals, therefore avoid Atlantic salmon or other fish or shellfish not labeled as wild-caught. Large ocean fish such as tuna, swordfish, king mackerel or bluefish may be high in mercury too.
- Insufficient zinc forces an increase in MTR activity and reduces methyl folate levels. This is possibly because zinc deficiency causes BHMT inhibition and therefore reduces the alternative route for SAM recycling.
- It is also important to avoid foods which slow MTHFR and MTRR.

Supplements and Medications:

- Inhaled nitrous oxide aka 'laughing gas' (dental procedures, pre-op and maternity wards) damages vitamin B12.
- Cyanocobalamin may slow MTR as MTR needs methylated cobalamin.
- Although cyanocobalamin does not contain much cyanide, it uses up glutathione which could be used for better purposes, especially in those already deficient.

Cleans your MTR gene

Environment:

- Utilize chlorine filters for bath, shower and drinking as chlorine uses up glutathione.
- Create a low formaldehyde environment: instead of synthetic carpet, laminate flooring or furniture consider solid wood, concrete, cork, tile or real linoleum.
- One should also support environmental recommendations for MTHFR and MTRR.

Lifestyle: Exercise but do not overtrain.

Cleans your MTR gene, continued...

Food:

- Focus on vitamin B12, zinc and sulfur rich (for glutathione production) foods.
- Aim for balanced protein intake which is also called 'Nitrogen balanced'.
- If protein intake is too low, especially in pregnancy, breastfeeding or growing children, homocysteine levels may be too low (< 5 umol/L).
- Alaskan salmon is lower in heavy metals as are smaller fish like herring or sardines.
- One should also eat for a clean MTHFR and MTRR.

Supplements and Medications: Vegans, vegetarians and those with malabsorption issues (gastritis, etc.) may need methylcobalamin or hydroxocobalamin (B12) supplementation. Hydroxocobalamin neutralizes the toxicity of cyanide, therefore discontinue cyanocobalamin and switch to hydroxocobalamin. Consider zinc, methylfolate (L-5-MTHF) and betaine. Antioxidants such as liposomal glutathione, S-acetyl glutathione or PQQ (pyrroloquinoline quinone). One must also evaluate supplements which support MTHFR and MTRR.

THE MTRR GENE

The MTRR (methionine synthase reductase) gene expresses an enzyme which supports the MTR enzyme by restoring its B12 cofactor.

If MTRR is unable to restore the damaged vitamin B12, then the MTR enzyme cannot function and the methylation cycle is compromised.

In order for MTRR to repair oxidized vitamin B12, it needs three cofactors: FAD, a form of riboflavin (B2); NADP+, a form of niacin (B3) and S-adenosylmethionine (SAM). (Repair of the oxidized vitamin B12 cofactor occurs approximately once every 200 enzyme turnovers so not much SAM is used.)

The interaction between MTRR, MTR and MTHFR is significant and all three must be functioning well.

Dirties your MTRR gene

Lifestyle: High oxidative stress which may be caused by overtraining, low antioxidants, infections and the standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium, oxidized inflammatory fats, and low in fiber and good quality protein.

Supplements and Medications: Inhaled nitrous oxide aka laughing gas (dental procedures, pre-op and maternity wards) damages vitamin B12.

Cleans your MTRR gene

Food: Riboflavin (B2), niacin (B3) and B12 rich

Supplements and Medications: Optimize riboflavin (B2) levels and B12 levels using methylcobalamin or hydroxocobalamin. Very little SAM is used by MTRR so supplementing with SAMe is likely not needed. Consider SAM conserving nutrients such as creatine and phosphatidylcholine. Choose non-GMO soy or sunflower derived phosphatidylcholine. Consider antioxidants such as PQQ (pyrroloquinoline quinone), S-acetyl glutathione, liposomal glutathione and SOD (superoxide dismutase).

Notable variation:

SNP: **MTRR C524T rs1532268 (+/-, TC)**
This CT variant causes a lower affinity of MTRR for the MTR-cobalamin-complex, thereby decreasing the rate at which damaged cobalamin (B12) can be restored. This results in a decreased rate of homocysteine remethylation.

SNP: **MTRR G66A rs1801394 (+/+, GG)**
This GG variant causes a lower affinity of MTRR for the MTR-cobalamin-complex, thereby decreasing the rate at which damaged cobalamin (B12) can be restored. This results in a decreased rate of homocysteine remethylation.

THE TCN2 GENE

The TCN2 (transcobalamin II) gene expresses a protein which binds cobalamin (B12) once it has been absorbed through the intestines and the Intrinsic Factor-Vitamin B12 complex has been degraded. This transcobalamin II protein transports cobalamin from the bloodstream to cells throughout the body.

Dirties your TCN2 gene

Lifestyle: Poor digestion, low stomach acid, increased age, malabsorptive disorders negatively impact overall vitamin B12 levels.

Food: Inadequate B12 from food sources (vegans, vegetarians, poor diet in general); foods or beverages enriched with synthetic folic acid

Supplements and Medications: Synthetic folic acid must be avoided because it appears to impact vitamin B12 binding to TCN2 thereby increasing risk of peripheral neuropathy.

Cleans your TCN2 gene

Food: B12 rich

Supplements and Medications: Optimize with a combination of methylcobalamin (methyl B12) and adenosylcobalamin (adeno B12) as needed. Oral or sublingual administration of adequate doses of methylcobalamin and adenosylcobalamin are comparable to intramuscular injection in raising serum B12. If methyl B12 or adeno B12 are not well tolerated, consider hydroxocobalamin.

Notable variation:

SNP: **TCN2 rs526934 (+/-, AG)**

This GA variant may cause decreased cellular and plasma concentration of TCN2, resulting in lower cellular availability of vitamin B12.

THE MAT1A GENE

The MAT1A (methionine adenosyl transferase 1A) gene expresses an enzyme which transfers adenosine (from ATP) to methionine to form S-adenosylmethionine (SAM).

MAT1A requires magnesium and potassium as cofactors and the substrate methionine, which is a sulfur-containing amino acid supplied from ingested and absorbed protein.

SAM is your body's primary methyl donor, and supports over 200 methylation reactions, so if MAT1A's formation of SAM is not functioning well, then neither are 200 other enzymatic reactions.

Some key enzymes requiring SAM are COMT (estrogen and dopamine metabolism), GAMT (creatine formation), ASMT (melatonin formation), PEMT (phosphatidylcholine formation), PNMT (norepinephrine metabolism), HNMT (histamine metabolism) and elimination of arsenic, to name a few.

As you can see, a lack of SAM is a very significant problem.

💩 Dirties your MAT1A gene

Environment: Carbon tetrachloride

Lifestyle: Limit alcohol and caffeine. Work with your healthcare provider to identify and treat intestinal dysbiosis; infections including hepatitis B and hepatitis C; or hypoxia.

Food: Excessive protein intake (more than 1 or 2 grams of protein per kg [2.2 lbs] of body weight). Excessive caffeine intake causes loss of magnesium and potassium which are both needed as cofactors.

Supplements and Medications: Avoid acetaminophen (Tylenol), inhaled nitrous oxide aka laughing gas (dental procedures, pre-op and maternity wards); antacids (as they suppress stomach acid and thereby reduce protein absorption and lower methionine which is needed to make SAM).

Cleans your MAT1A gene

Lifestyle: Consider intermittent fasting or short term fasting especially during times of high homocysteine as it lowers methionine, the substrate of homocysteine. Long term fasting (many days) may be problematic due to protein deficiency.

Food: Focus on magnesium and potassium rich sources. Consume, digest and absorb appropriate amounts of protein (approximately 0.8 grams of protein per kg [2.2 lbs] of body weight).

Notable variation:

While no notable variation was found, we are presenting this gene's information to you because it's so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

Cleans your MAT1A gene, continued...

Supplements and Medications:

- Optimize magnesium and potassium. Studies indicate that 99% of women and 90% of men are potassium deficient. Electrolytes may be a great source of potassium.
- Use appropriate probiotics and antimicrobials as needed.
- Liposomal glutathione, PQQ (pyrroloquinoline quinone) or S-acetyl glutathione as needed.
- Digestive enzymes and protein powders may be needed if protein absorption is an issue.

THE PEMT GENE

The PEMT (phosphatidylethanolamine N-methyltransferase) gene expresses an enzyme that generates phosphatidylcholine (PC) from phosphatidyl ethanolamine (PE).

PC is crucial for maintaining a healthy cell membrane and permeability as well as bile flow, liver health, muscle health and brain development.

PEMT is stimulated by estradiol so men as well as women with low estradiol may have lower PC synthesis.

Bile should consist of 10 parts PC to 1 part cholesterol. If this ratio is off, gallstones may occur.

PC is also high in breastmilk. If low, it may lead to mastitis.

PEMT needs a lot of S-adenosylmethionine (SAM) to function. Thus, PEMT may be greatly impacted by other genes that require SAM: GAMT, COMT and HNMT or generate SAM: MTHFR, MAT1A, MTR, MTRR and CBS.

Dirties your PEMT gene

Lifestyle:

- Pregnancy and breastfeeding utilizes large amounts of phosphatidylcholine (PC).
- Type 1 diabetes tends to depress PC production.
- Estrogen promotes expression of this gene, therefore post-menopausal women are at higher risk due to potentially lower estrogen levels.

Food: High fat diets or ketogenic diets utilize significant amounts of bile. Bile flow requires 10 parts PC and 1 part cholesterol. Gallstones form if this ratio is imbalanced.

Supplements and Medications:

- Watch for symptoms of depression from phosphatidylcholine supplementation which may result from an imbalanced ratio of acetylcholine to serotonin. Choose non-GMO soy or sunflower derived phosphatidylcholine.
- Some medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Notable variation:

SNP: **PEMT G5465A rs7946 (+/+, TT)**

This TT variant has approximately 30% lower PEMT activity. Carriers of this variant may benefit from betaine and choline rich foods.

Cleans your PEMT gene

Lifestyle: Healthy estrogen levels in women of reproductive age help promote optimal expression of PEMT. Pregnancy increases estrogen levels which may further enhance expression.

Food: Adequate protein intake; foods rich in betaine, choline, vitamin E

Supplements and Medications: Consider choline or phosphatidylcholine (PC) supplementation especially for pregnant or breastfeeding women, growing children, non-egg eating vegetarians, and vegans. 800 mg of choline or PC daily is recommended during pregnancy or breastfeeding.

However, be aware that excessive choline intake may exacerbate underlying insulin resistance. Consider betaine, vitamin E, SAMe (S-adenosylmethionine).

If depression results from PC or choline supplementation: consider uridine, 5-hydroxytryptophan (5-HTP) or inositol along with PQQ (pyrroloquinoline quinone) and liposomal curcumin.

For postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus) if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use. This strategy for PEMT may not be useful if you possess the T variant of rs3760188 (not present).

THE GAMT GENE

The GAMT (guanidinoacetate N-methyltransferase) gene expresses an enzyme which catalyzes the reaction that converts guanidinoacetate to creatine. It requires SAM as a cofactor.

Creatine is utilized heavily by the brain and muscles. If creatine levels are low due to low dietary intake of meat or a poorly functioning GAMT enzyme, one may experience a variety of issues. These issues may range from speech delay, movement disorders, muscle weakness, attention difficulties and reduced cognitive ability.

Every day, 1% to 2% of muscle creatine breaks down into creatinine and is eliminated via the kidneys. Men generally tend to have higher concentrations of creatinine than women because they have more skeletal muscle. For example, about 2 grams of creatine is eliminated as creatinine via the kidneys in 70 kg males of average age between 20 and 39.

Dietary intake of meat and fish can replace some of the lost creatine; however, the rest must be produced via the GAMT enzyme. Homocysteine levels may be increased due to a constant need of creatine synthesis. This is because when SAM is used by GAMT to make creatine, the SAM becomes homocysteine (in two biochemical steps).

About 20-30% of your body's arginine is also consumed to produce creatine. This is an important side note as your NOS3 enzyme (in Biopterin Pathway) also requires arginine to produce nitric oxide. If you're putting a large burden of synthesizing creatine via your GAMT enzyme vs dietary intake of creatine, you may also be dirtying your NOS3 gene.

💩 Dirties your GAMT gene

Environment: Avoid exposure to endocrine disrupting chemicals such as plasticisers, bisphenol A (BPA) and phthalates.

Lifestyle: Alcohol. Vegans and vegetarians place a high demand on the GAMT enzyme as they are not consuming creatine from meat and fish. This may lead to increased homocysteine levels and reduced creatine levels in their brain and muscle. The ketogenic lifestyle may place a high burden on the GAMT enzyme due to low dietary intake of meat and fish.

Food: Starvation, fasting, blood sugar dysregulation can all stress GAMT.

Notable variation:

While your genetic test didn't cover any notable variants in this gene, we are presenting this gene's information to you because it's so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

Cleans your GAMT gene

Food: Protein-containing meals, especially as meat and fish, provide sufficient methionine and arginine needed to support creatine synthesis.

Supplements and Medications: Consider S-adenosylmethionine (SAMe) as it is the cofactor for GAMT. If homocysteine levels are elevated, do not supplement with SAMe until homocysteine levels normalize.

Since GAMT makes creatine, one can directly supplement with creatine in a magnesium creatine complex form. Creatine supplementation may reduce homocysteine levels as well by 25%. This is because SAM is needed to make creatine. After SAM donates its methyl group to GAMT, the SAM becomes SAH. SAH turns into homocysteine. So by supplementing directly with creatine, one does not need to use up their SAM thereby conserving it. By conserving the use of SAM, homocysteine isn't generated.

In the rare genetic diseases of GAMT deficiency, creatine supplementation is needed lifelong. However unrecognized mild creatine deficiencies can exist more commonly. In these cases, creatine may make a significant difference. It is important to realize supplementation of creatine is needed long term to restore depleted creatine pools. Therefore a therapeutic trial of creatine should last several months before evaluating its benefit, not just days.

Creatine is poorly absorbed. To help overcome this, mix your creatine powder supplement in filtered water and place inside a water bottle. Sip it throughout the day. This way you are increasing absorption while reducing digestive upset of gas and bloating. Creatine supplementation in adults at 5 grams a day appears safe and does not negatively impact normally functioning kidneys. Adding L-ornithine and/or alpha-ketoglutarate may be needed if one is demonstrating higher ammonia levels due to a slowed GAMT enzyme.

THE ALDH7A1 GENE

The ALDH7A1 (aldehyde dehydrogenase family member A1) gene expresses an enzyme which metabolizes betaine aldehyde to betaine. It requires niacin (B3) as a cofactor.

The ALDH7A1 enzyme also protects cells from oxidative stress by degrading aldehydes generated via alcohol metabolism, lipid peroxidation and other causes of oxidative stress.

Aldehydes can be very damaging compounds so it is vital to clear them from the body. To underscore this point, ALDH7A1 doubles in activity during late pregnancy, a time of increased oxidative stress, and returns to normal levels postpartum.

Dirties your ALDH7A1 gene

Environment: Minimize air pollutants (formaldehyde, acetaldehyde, acrolein) which are mainly from fuel combustion (natural gas, gas, diesel).

Lifestyle: Dehydration, hydrogen peroxide

Cleans your ALDH7A1 gene

Environment: Utilize air filters, especially choosing the 'Recirculation of Air' option for in your car versus the "Outside Air" option that allows in vehicle exhaust while driving. Be sure to use high smoke point oils such as avocado oil or ghee, cook in a well-ventilated area and use the extractor hood.

Lifestyle: Optimize hydration by drinking water with appropriate electrolyte balance. Hydration is not just drinking water but the process of causing something to absorb water. Electrolytes enhance water absorption inside cells.

Food: Niacin (B3), pyridoxine (B6), thiamine (B1), betaine rich

Supplements and Medications: Optimize niacin (B3), thiamine (B1) and pyridoxine (B6). Aldehydes damage B1, so additional B1 will be needed if aldehydes are high.

Notable variation:

While no notable variation was found, we are presenting this gene's information to you because it's so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

THE BHMT GENE

The BHMT (betaine-homocysteine S-methyltransferase) gene expresses an enzyme, primarily located in the liver and kidney, which is important for homocysteine metabolism.

Requiring zinc as a cofactor, it catalyzes the transfer of a methyl group (-CH3) from trimethylglycine (TMG aka betaine) to homocysteine to produce dimethylglycine (DMG) and methionine.

If the MTR/MTRR gene complex is slowed for any reason, BHMT steps up as an important alternative route for homocysteine recycling.

This is a perfect example of how the body has back-up systems in place in case one fails.

Dirties your BHMT gene

Lifestyle: Vegan or vegetarian diet can hamper this gene as choline is found mainly in meat, poultry, fish and dairy. Hypo or hypertonic dehydration (water deprivation, excessive sweating, high blood sugar, heat stroke, heat exhaustion, vomiting, diarrhea, burns, muscle damage, low sodium diet); blood sugar dysregulation, hyperthyroidism can all impede BHMT.

Food: Low choline/taurine diet (low protein with low animal meat or organ content), low betaine intake

Supplements and Medications: Dimethylglycine (DMG) is known to potentially increase homocysteine due to feedback inhibition. Low pyridoxine (B6), acetaminophen (Tylenol), some diuretics can also interfere. Consult your healthcare provider or pharmacist.

Cleans your BHMT gene

Lifestyle: Optimize hydration by drinking water with appropriate electrolyte balance. Hydration is not just drinking water but the process of causing something to absorb water. Electrolytes enhance water absorption inside cells.

Food: Choline, taurine, betaine, zinc and pyridoxine (B6) rich

Supplements and Medications: Optimize zinc and pyridoxine (B6). Consider TMG (betaine; trimethylglycine), choline bitartrate. TMG in gram doses may be very effective in lowering stubbornly elevated levels of homocysteine. TMG may also help support weakened kidneys as kidneys are naturally high in betaine when healthy.

If TMG supplementation does not result in lower homocysteine or improved mental symptoms, DMG (dimethylglycine) supplementation may be useful instead. DMG is not recommended for pregnant or nursing mothers due to lack of research.

Notable variation:

SNP: **BHMT 716G>A rs3733890 (+/-, AG)**

This GA variant has a lower Km value, greater stability and high substrate affinity which means it can work faster compared to wild type. This allows for a greater capacity to recycle homocysteine via the "short route" in the liver.

THE PON1 GENE

The PON1 (serum paraoxonase 1) gene expresses an enzyme which acts as a potent antioxidant requiring calcium as a cofactor.

In the SAM cycle, PON1 converts harmful homocysteine thiolactone back to homocysteine.

PON1 also helps to neutralize hydrogen peroxide (H_2O_2), and plays a major role in preventing the formation of oxidized LDL which could contribute to atherosclerosis.

In addition, PON1 has the ability to degrade the toxic metabolites of a variety of organophosphate insecticides. PON1 also metabolizes substrates such as glucuronide drugs, cyclic carbonates, estrogen esters, and other lactones such as statin medications.

Dirties your PON1 gene

Environment: Minimize ionizing radiation and environmental chemicals such as organophosphate pesticides (known to contribute to ADHD in children), polyaromatic hydrocarbons (PAH), carbon tetrachloride, non-dioxin-like PCBs and dichloroacetic acid (a major by-product of water disinfection by chlorination).

Avoid the Dirty Dozen as explained by Environmental Working Group.

Avoid smoke from any source such as incense, woodsmoke, air pollution, vehicle exhaust, cooking without an extractor hood especially with low smoke point oils.

Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections; heavy metal exposures including mercury, copper, lanthanum, lead, cadmium, barium.

Lifestyle: In general, males have less PON1 activity and are therefore more susceptible to environmental factors that inhibit PON1 activity. A high LDL:HDL ratio, thyroid, liver or kidney disease can also all stress PON1.

Food: PON1 is especially sensitive to damage from the standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium, oxidized inflammatory fats, and low in fiber and good quality protein.

Supplements and Medications: Some medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Notable variation:

SNP: **PON1 575A>G rs662 (+/+, TT)**

The TT variant appears to be more efficient at preventing the oxidation of LDL (oxidized LDL increases the risk of cardiovascular disease) but worse at neutralizing homocysteine thiolactone (a harmful metabolite of homocysteine thought to be atherogenic). TT individuals may have lower ability to detoxify organophosphates paraoxon and diazoxon (thus may be at a greater risk for cancer and neurodegenerative disease risk) but are faster at detoxifying the nerve agents soman and sarin. TT carriers, especially males, may be more susceptible to environmental chemical exposures: CCl4, non-dioxin-like PCBs, pesticides, dichloroacetic acid (a major by-product of water disinfection by chlorination), ionizing radiation and smoking.

SNP: **PON1 L55M rs854560 (+/+, TT)**

The TT variant may decrease enzyme expression, resulting in approximately 30-50% less enzyme activity. TT genotypes may have lower ability to detoxify organophosphate pesticides (thus may be at greater risk for cancer and neurodegenerative disease). TT carriers, especially males, may be more likely susceptible to environmental chemical exposures: CCl4, non-dioxin-like PCBs, pesticides, dichloroacetic acid (a major by-product of water disinfection by chlorination), ionizing radiation and smoking.

A PON1 575A>G/L55M Haplotype

HOM 575A>G TT and HOM L55M TT exhibited less than 50% PON1 activity in regard to organophosphate metabolism compared to wild type. This haplotype is vulnerable to pesticide exposures. Eating organically and avoidance of chemical exposures is recommended. May be more prone to environmentally-caused ADHD, especially males, due to increased sensitivity to organophosphates. Pregnant women may be more prone to pesticides affecting their thyroid function and increasing neurodevelopmental, cognitive and behavioral disorders in offspring.

Gene	rsID	Alias	Variant Allele	Call
PON1	rs662	575A>G	T	TT
PON1	rs854560	L55M	T	TT

Cleans your PON1 gene

Environment: Utilize air filters, especially choosing the 'Recirculation of Air' option for in your car versus the "Outside Air" option that allows in vehicle exhaust while driving. Be sure to use high smoke point oils such as avocado oil or ghee, cook in a well-ventilated area and use the extractor hood.

Lifestyle: High intensity interval training (HIIT) as well as moderate, regular exercise like walking increases PON1 activity, especially when undertaken regularly.

Food:

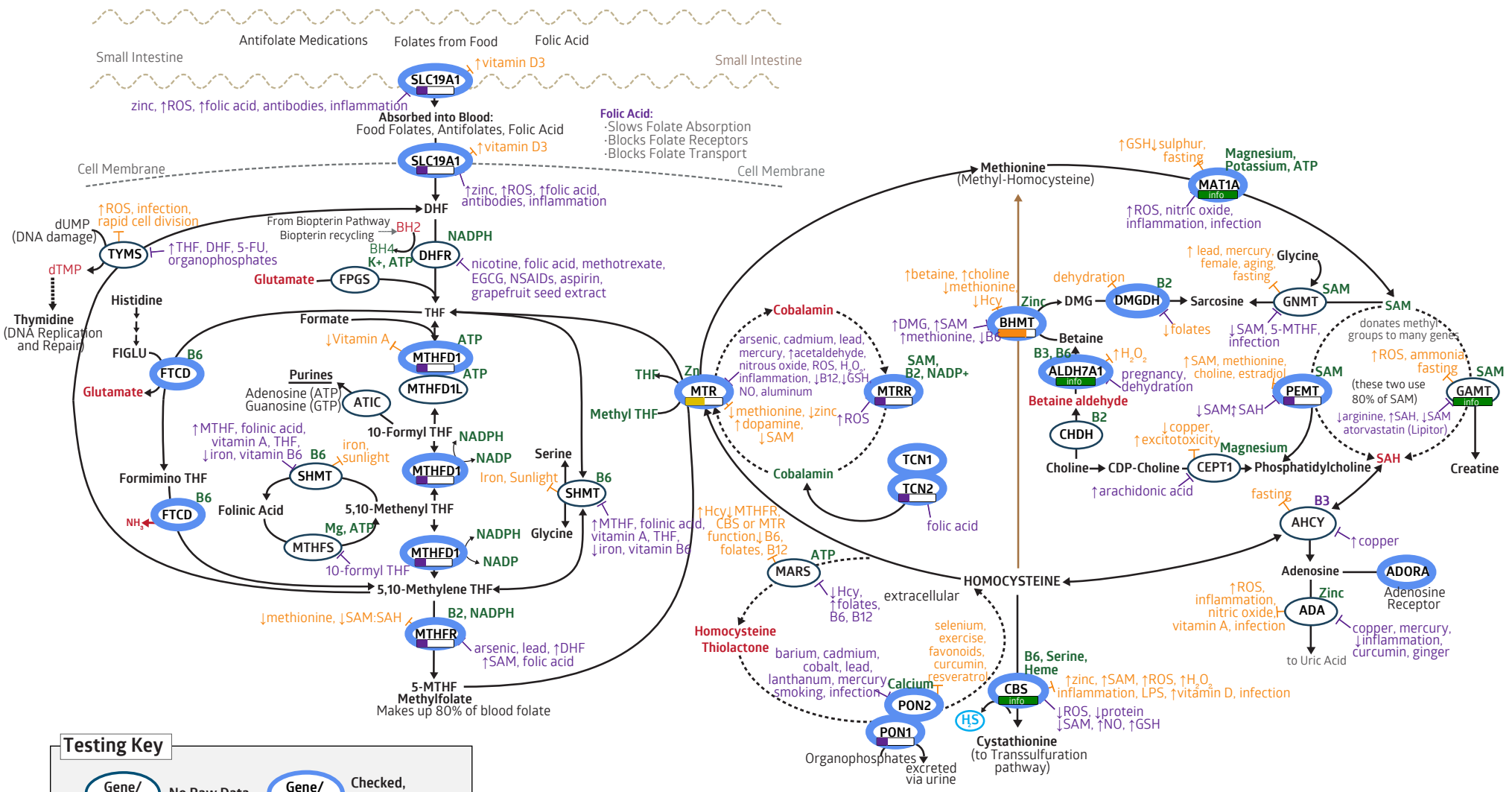
- Focus on calcium, selenium, lycopene rich sources. Opt for a Mediterranean diet rich in extra virgin olive oil, cold water fish, legumes, nuts, seeds, fruits and vegetables.
- Choose meat cooking methods that employ lower, indirect heat such as braising or stewing which decrease polyaromatic hydrocarbon (PAH) formation.
- Polyaromatic hydrocarbons from chargrilling meat may also be reduced by marinating meats for 4 hours prior to grilling in beer, vinegar or tea (both green or black) based sauces including lemon, onions, garlic, or alternatively: spraying meat with culinary vinegar prior to grilling. (Polyaromatic hydrocarbon formation was decreased by almost 80% using white wine vinegar, 66% by red wine and cider vinegar.)
- Use an extractor hood while cooking and high-smoke point oils like ghee or avocado oil.

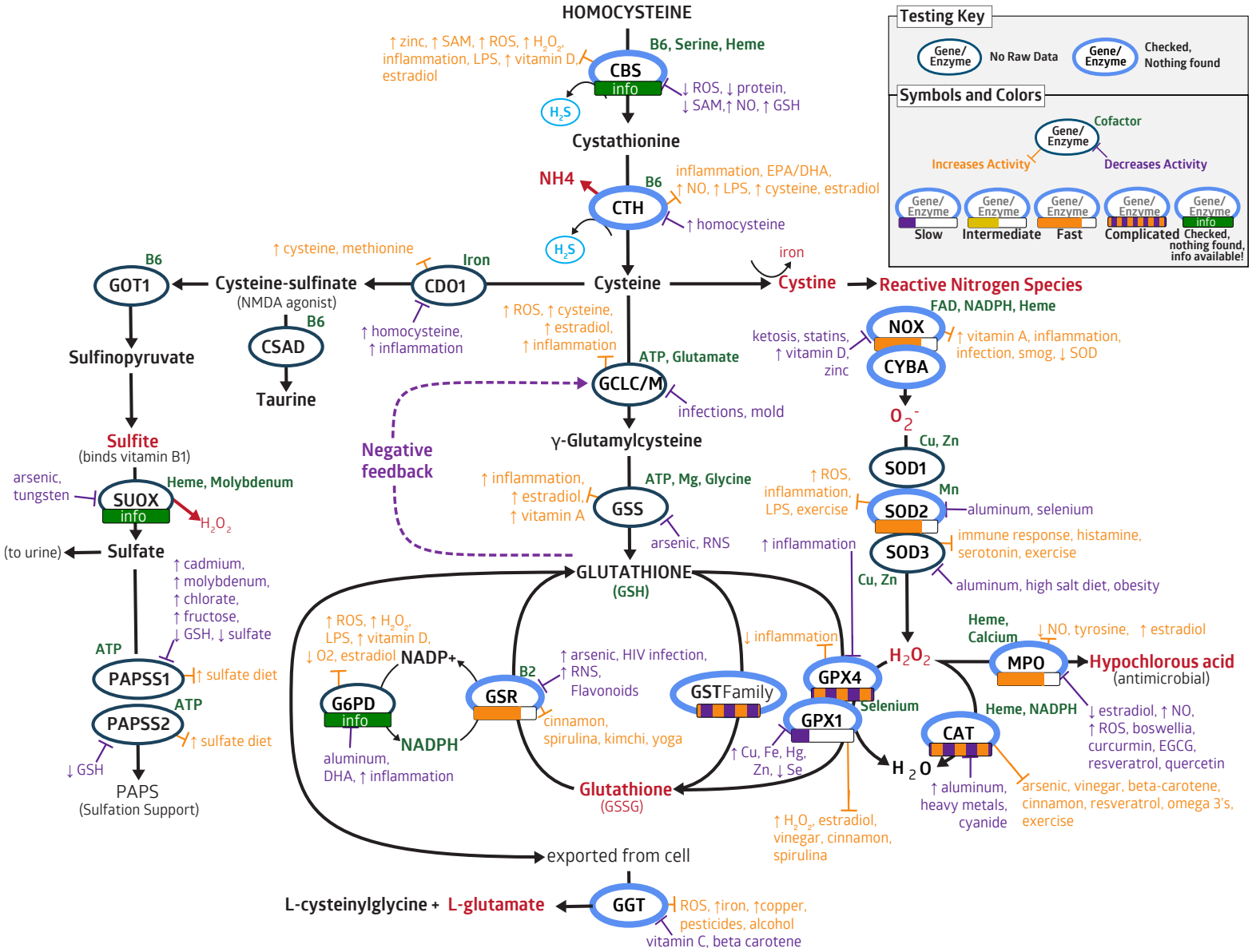
Supplements and Medications:

- Consider omega-3 fish oils, N-acetylcysteine (NAC), quercetin, L-carnitine, low dose aspirin, *Lactobacillus spp.*, artichoke, berberine, curcumin, licorice, resveratrol, *Ilex paraguariensis* (yerba mate) and pomegranate, vitamin E (alpha-tocopherol). Use methylation support supplements as needed to optimize homocysteine levels.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause and other indications for its use. Estrogen indirectly supports increased PON1 activity by raising HDL levels, as well as increasing PON1 activity.

THE CBS GENE

The complete discussion of this gene is under Glutathione.


Antifolate Medications
Folates from Food
Folic Acid
Small Intestine
Small Intestine
SLC19A1
↑vitamin D3
zinc, ↑ROS, ↑folic acid, antibodies, inflammation
Absorbed into Blood:
Food Folates, Antifolates, Folic Acid
Folic Acid:
·Slows Folate Absorption
·Blocks Folate Receptors
·Blocks Folate Transport
Cell Membrane
Cell Membrane
↑zinc, ↑ROS, ↑folic acid, antibodies, inflammation
DHF
From Biopterin Pathway
Biopterin recycling
BH2
BH4
K+, ATP
NADPH
DHFR
nicotine, folic acid, methotrexate, EGCG, NSAIDs, aspirin, grapefruit seed extract
↑ROS, infection, rapid cell division
dUMP
(DNA damage)
TYMS
↑THF, DHF, 5-FU, organophosphates
dTMP
Thymidine
(DNA Replication and Repair)
Glutamate
FPGS
THF
Histidine
FIGLU
B6
FTCD
Glutamate
Formimino THF
B6
FTCD
NH3
Formate
↓Vitamin A
ATP
MTHFD1
MTHFD1L
ATP
Purines
Adenosine (ATP)
Guanosine (GTP)
ATIC
10-Formyl THF
NADPH
↑MTHF, folinic acid, vitamin A, THF, ↓iron, vitamin B6
B6
SHMT
iron, sunlight
MTHFD1
NADP
Folinic Acid
5,10-Methenyl THF
Mg, ATP
MTHFS
10-formyl THF
NADPH
MTHFD1
NADP
5,10-Methylene THF
Serine
Iron, Sunlight
B6
SHMT
Glycine
↑MTHF, folinic acid, vitamin A, THF, ↓iron, vitamin B6
↓methionine, ↓SAM:SAH
B2, NADPH
MTHFR
arsenic, lead, ↑DHF ↑SAM, folic acid
5-MTHF
Methylfolate
Makes up 80% of blood folate
THF
Zn
Methyl THF
MTR
Cobalamin
arsenic, cadmium, lead, mercury, ↑acetaldehyde, nitrous oxide, ROS, H2O2, inflammation, ↓B12, ↓GSH, NO, aluminum
↓methionine, ↓zinc, ↑dopamine, ↓SAM
↑ROS
MTRR
SAM, B2, NADP+
Cobalamin
TCN1
TCN2
folic acid
↑Hcy, ↓MTHFR, CBS or MTR function, ↓B6, folates, B12
MARS
ATP
↓Hcy, ↑folates, B6, B12
extracellular
Homocysteine
Thiolactone
barium, cadmium, cobalt, lead, lanthanum, mercury, smoking, infection
selenium, exercise, favonoids, curcumin, resveratrol
Calcium
PON2
PON1
Organophosphates
excreted via urine
Methionine
(Methyl-Homocysteine)
↑GSH↓sulphur, fasting
Magnesium, Potassium, ATP
MAT1A
info
↑ROS, nitric oxide, inflammation, infection
↑betaine, ↑choline ↓methionine, ↓Hcy
Zinc
BHMT
↑DMG, ↑SAM ↑methionine, ↓B6
Betaine
DMG
dehydration
B2
DMGDH
Sarcosine
↓folates
↑ lead, mercury, female, aging, fasting
Glycine
GNMT
↓SAM, 5-MTHF, infection
SAM
donates methyl groups to many genes
↑ROS, ammonia, fasting
(these two use 80% of SAM)
↓arginine, ↑SAH, ↓SAM atorvastatin (Lipitor)
GAMT
info
Creatine
B3, B6
ALDH7A1
info
↑H2O2
pregnancy, dehydration
Betaine aldehyde
B2
CHDH
Choline
CDP-Choline
CEPT1
Phosphatidylcholine
↑arachidonic acid
↑SAM, methionine, choline, estradiol
PEMT
↓SAM↑SAH
↓copper, ↑excitotoxicity
Magnesium
SAH
fasting
B3
AHCY
↑copper
HOMOCYSTEINE
Adenosine
ADORA
Adenosine Receptor
↑ROS, inflammation, nitric oxide, vitamin A, infection
Zinc
ADA
copper, mercury, ↓inflammation, curcumin, ginger
to Uric Acid
B6, Serine, Heme
CBS
info
↑zinc, ↑SAM, ↑ROS, ↑H2O2, inflammation, LPS, ↑vitamin D, infection
↓ROS, ↓protein ↓SAM, ↑NO, ↑GSH
H2S
Cystathionine
(to Transsulfuration pathway)
Testing Key
Gene/ Enzyme
No Raw Data
Gene/ Enzyme
Checked, Nothing found
Symbols and Colors
Cofactor
Gene/ Enzyme
Increases Activity
Decreases Activity
Gene/ Enzyme
Slow
Gene/ Enzyme
Intermediate
Gene/ Enzyme
Fast
Gene/ Enzyme
Complicated
Gene/ Enzyme
info
Checked, nothing found, info available!


HOMOCYSTEINE
↑ zinc, ↑ SAM, ↑ ROS, ↑ H2O2, inflammation, LPS, ↑ vitamin D, estradiol
B6, Serine, Heme
CBS
info
↓ ROS, ↓ protein, ↓ SAM,↑ NO, ↑ GSH
H2S
Cystathionine
NH4
B6
CTH
inflammation, EPA/DHA, ↑ NO, ↑ LPS, ↑ cysteine, estradiol
↑ homocysteine
H2S
↑ cysteine, methionine
Iron
B6
GOT1
Cysteine-sulfinate
(NMDA agonist)
CDO1
Cysteine
iron
Cystine
Reactive Nitrogen Species
B6
CSAD
Taurine
↑ homocysteine, ↑ inflammation
↑ ROS, ↑ cysteine, ↑ estradiol, ↑ inflammation
ATP, Glutamate
GCLC/M
infections, mold
Sulfinopyruvate
Negative feedback
γ-Glutamylcysteine
FAD, NADPH, Heme
NOX
CYBA
ketosis, statins, ↑ vitamin D, zinc
↑ vitamin A, inflammation, infection, smog, ↓ SOD
O2-
Cu, Zn
SOD1
Mn
SOD2
aluminum, selenium
SOD3
immune response, histamine, serotonin, exercise
aluminum, high salt diet, obesity
Sulfite
(binds vitamin B1)
arsenic, tungsten
SUOX
info
Heme, Molybdenum
H2O2
(to urine)
Sulfate
↑ inflammation, ↑ estradiol, ↑ vitamin A
ATP, Mg, Glycine
GSS
arsenic, RNS
↑ ROS, inflammation, LPS, exercise
↑ inflammation
GLUTATHIONE
(GSH)
Cu, Zn
↑ cadmium, ↑ molybdenum, ↑ chlorate, ↑ fructose, ↓ GSH, ↓ sulfate
ATP
PAPSS1
↑ sulfate diet
ATP
PAPSS2
↑ sulfate diet
↓ GSH
PAPS
(Sulfation Support)
↑ ROS, ↑ H2O2, LPS, ↑ vitamin D, ↓ O2, estradiol
NADP+
G6PD
info
NADPH
aluminum, DHA, ↑ inflammation
GSR
B2
↑ arsenic, HIV infection, ↑ RNS, Flavonoids
cinnamon, spirulina, kimchi, yoga
GSTFamily
↓ inflammation
GPX4
Selenium
GPX1
↑ Cu, Fe, Hg, Zn, ↓ Se
Glutathione
(GSSG)
H2O2
Heme, Calcium
↓ NO, tyrosine, ↑ estradiol
MPO
Hypochlorous acid
(antimicrobial)
Heme, NADPH
CAT
↓ estradiol, ↑ NO, ↑ ROS, boswellia, curcumin, EGCG, resveratrol, quercetin
H2O
↑ aluminum, heavy metals, cyanide
arsenic, vinegar, beta-carotene, cinnamon, resveratrol, omega 3's, exercise
↑ H2O2, estradiol, vinegar, cinnamon, spirulina
exported from cell
L-cysteinylglycine + L-glutamate
GGT
ROS, ↑iron, ↑copper, pesticides, alcohol
vitamin C, beta carotene
Testing Key
Gene/Enzyme
No Raw Data
Checked, Nothing found
Symbols and Colors
Cofactor
Increases Activity
Decreases Activity
Slow
Intermediate
Fast
Complicated
Checked, nothing found, info available!

THE CBS GENE

The CBS (cystathionine beta-synthase) gene expresses an enzyme which catalyzes the conversion of homocysteine to cystathionine by the addition of serine requiring pyridoxine (B6) and heme as cofactors. CBS is the first rate-limiting step in the Glutathione Pathway.

CBS controls whether homocysteine is conserved for the SAM cycle, by recycling homocysteine back to S-adenosylmethionine (SAM) or whether homocysteine is removed from the cycle by being shunted into the Glutathione Pathway.

A byproduct of CBS' conversion of homocysteine to cystathionine is hydrogen sulfide (H_2S), which is an important synaptic modulator and neuroprotectant in the brain. H_2S is also involved in blood pressure regulation and healthy respiratory function.

Hydrogen sulfide levels must be optimized. Too low and one may experience hypertension or difficulty breathing (asthma). Too high and one may experience fatigue, headaches, irritability.

💩 Dirties your CBS gene

Environment: High levels of hydrogen sulfide are toxic to humans. Since the CBS enzyme produces hydrogen sulfide, an excessive amount of hydrogen sulfide may be produced especially if the environment is also contributing to the levels. Tropical areas may have higher amounts of hydrogen sulfide in the air and water. Sewers can also vent fumes high in hydrogen sulfide.

Lifestyle: Peroxynitrite from an uncoupled NOS3 enzyme increases CBS expression. In fact, any reactive oxygen species increases CBS expression in order to stimulate production of glutathione. However, a prolonged increased CBS expression may lower vitamin B6 levels, lower homocysteine too much (< 5 umol/L), increase hydrogen sulfide levels excessively, and burden other downstream enzymes such as SUOX and GSR.

Increased burden on SUOX may then in turn increase sulfites and deplete molybdenum. Increased burden on GSR may deplete riboflavin thereby increasing oxidized glutathione.

People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may have impaired CBS function as heme is the required cofactor for this enzyme.

Also, many parasites and gram negative bacteria need heme to reproduce and cause infection. These pathogens must synthesize their own heme or steal heme from the host. Thus, untreated chronic parasite or bacterial infections may create a heme deficiency. (Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.)

Hydrogen sulfide producing bacteria may increase/elevate hydrogen sulfide levels to unhealthy levels. Discuss with your healthcare provider if you exhibit "rotten egg" smelling gas, diarrhea, or other digestive issues.

Intensive exercise and overtraining increase inflammation which may push the CBS enzyme to work excessively.

Notable variation:

While no notable variation was found, we are presenting this gene's information to you because it's so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

Dirties your CBS gene, continued...

Food: Low protein diets may impair CBS enzyme from functioning from lack of substrate, homocysteine. Conversely, high protein, GAPS and Paleo diets may instead overwhelm the CBS enzyme with homocysteine due to increased methionine, cysteine and sulfur levels.

While these nutrients are necessary and supportive in the right amounts, they may be harmful when in excess or in short supply. The issue is quantity: a kale smoothie with two eggs and broccoli for breakfast is a perfect example of excessive cysteine and sulfur. Not everyone can tolerate a green smoothie or a high protein diet.

Supplements and Medications: Consider using *Saccharomyces boulardii* while using antibiotics and probiotics after a course of antibiotics. Limit acetaminophen (Tylenol). If the CBS gene is overtaxed, intake of sulfur-containing supplements such as N-acetylcysteine (NAC), methylsulfonylmethane (MSM) may be problematic. Maternal folic acid supplementation decreased expression of CBS.

Cleans your CBS gene

Environment: Avoid areas with higher levels of hydrogen sulfide.

Lifestyle: Exercise at a sustainable level with ability to fully recover within 24-48 hours.

Food:

- Focus on heme, iron, zinc, pyridoxine (B6) and vitamin D rich sources, and strive for protein intake at about 0.8 grams per kg (2.2 lbs) of body weight.
- Protein intake drives up homocysteine, so if homocysteine levels are elevated above > 8 umol/L in adults, reduce protein intake by the amount recommended by your healthcare provider.
- Find a level of sulfur-containing food consumption that agrees with your unique constitution. If consuming too much sulfur or protein, you may begin to smell like sulfur - skin, breath, stool, urine, flatulence. This is a sign to reduce intake slightly and discuss with your healthcare provider other potential causes.
- If the CBS enzyme is unresponsive to vitamin B6, consider betaine rich foods.

Supplements and Medications: Optimize pyridoxine (B6), glutathione, iron, zinc, vitamin D, probiotics. If the CBS enzyme is unresponsive to vitamin B6, consider betaine (TMG) or choline (but not in excessive amounts). If excessive hydrogen sulfide levels are present, use hydroxocobalamin (B12) to help reduce it. The element molybdenum and calcium-D-glucarate are very important for reducing sensitivity to sulfites and sulfur. Liposomal glutathione may also slow down a fast CBS enzyme, especially if hydrogen peroxide levels are stimulating it. PQQ (pyrroloquinoline quinone) may also help reduce oxidative stress and thereby slow an overexpressed CBS gene. Using anti-inflammatories, such as curcumin, may assist in balancing an over-active CBS.

THE SUOX GENE

SUOX (sulfite oxidase) gene expresses an enzyme residing in the mitochondria which oxidizes sulfite to sulfate. It uses heme and molybdenum as cofactors.

SUOX helps regulate the level of sulfite in the body. It is also an important enzyme in the generation of 3′-phosphate 5′-phosphosulfate (PAPS). PAPS is a cofactor for SULT enzymes which link sulfate groups to steroid hormones and endocrine disruptors. Many of these compounds are subsequently removed from the body in the bile and eliminated via the stool. However, some of these steroid sulphates are transported in plasma and released at the surface of target cells as needed. SUOX thus plays an important role in both detoxification, steroid hormone balance and hormone activity.

If SUOX isn't working well, this may have a number of consequences:

First, sulfation reactions that require PAPS will be slowed. This leads to a reduction in sulfur detoxification capacity and possible hormone imbalance.

Second, sulfite levels will increase. This may lead to sulfite intolerance in people. Sulfite intolerance can cause allergic symptoms such as breathing difficulties, dizziness, nausea, flushing, urticaria (hives), dermatitis or eczema. There is no known treatment for sulfite intolerance; however, if one cleans their SUOX gene, it only makes sense the sulfite levels will decrease and reduce the intolerance.

When sulfite levels are high, people are less likely to tolerate sulfur-containing foods such as protein and cruciferous vegetables, and to struggle with sulfur-based supplements (glutathione, NAC, MSM). Sulfites are also high in wine.

Additionally, increased sulfite levels are known to increase glutamate in the brain. This is caused by sulfites directly inhibiting the expression of the glutamate dehydrogenase (GDH) enzyme. Elevated glutamate levels lead to headaches, seizures, migraines, irritability, insomnia.

Commonly, many health professionals believe that GAD genetic variants are responsible for elevated glutamate. GAD is the enzyme that converts glutamate to GABA. While there may be some weak evidence for this, one must understand more common causes of elevated glutamate. Genetic variants of the SUOX gene are quite rare which is why we do not report any. StrateGene is more than reporting SNPs which is why we provide information on how to support your SUOX gene with lifestyle, food, environment and supplements.

Notable variation:

While your genetic test didn't cover any notable variants in this gene, we are presenting this gene's information to you because it's so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

💩 Dirties your SUOX gene

Environment:

- Avoid exposure to endocrine disrupting chemicals such as plasticisers, bisphenol A (BPA) and phthalates.
- Environmental exposure to tungsten has been shown to reduce SUOX activity and induce seizures in rats
- Sulfites are found in various medications, ointments, steroid creams.
- Sulfites are found in various cosmetics such as hair sprays, perfumes, blush, facial cleansers.
- Tap water is a common source of arsenic exposure.

Lifestyle:

- Evaluate heme deficiency. Many parasites and gram negative bacteria need the iron-containing heme, to reproduce and cause infection. Parasites and bacterial pathogens must either synthesize their own heme or acquire heme from the host. Thus, untreated chronic parasites and bacterial infections may create a heme deficiency.
- Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.
- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage due to low heme.
- Wine is high in sulfites and may dirty the SUOX gene very quickly.

Food: Avoid food grown in contaminated areas or down-wind of heavy industry.

Read food and drink labels for sulfites. Avoid foods with sulfites: dried fruits, dried vegetables, pickled onions, bottled soft drinks, fruit bars, dried coconut, commercial lime and lemon juice, grape juice, deli meats, crab, shrimp

Supplements and Medications: Molybdenum is a primary cofactor for SUOX. Be mindful that if too much molybdenum is taken, it may increase uric acid production. This may trigger gout. If taking higher amounts of molybdenum regularly, such as 10 grams, talk with your healthcare professional about monitoring your uric acid level.

Cleans your SUOX gene

Environment: Limit foods and drinks high in arsenic such as rice and some tap water, especially from wells. Use cosmetics without sulfites.

Lifestyle: Use glass rather than plastic containers for storing food and particularly avoid heating food in plastic containers.

Food: Choose foods rich in heme iron and molybdenum. Legumes, such as beans, lentils, and peas, are the richest sources of molybdenum. Grain products and nuts are considered good sources. Because the molybdenum content of plants depends on the soil molybdenum content and other environmental conditions, the molybdenum content of foods can vary considerably.

While animal products are generally low in molybdenum, they are a rich source of heme iron. So, a varied diet is advised.

Supplements and Medications: Optimize molybdenum. Consider molybdenum in liquid or capsule form as it is better absorbed. Do not use tablets. Avoid using molybdenum bound to ammonia known as ammonium molybdate. The form molybdenum glycinate is well-absorbed and without ammonia.

THE GSR GENE

The GSR (glutathione-disulfide reductase) gene expresses an enzyme which recycles oxidized glutathione (GSSG) back to its active reduced form (GSH) using riboflavin (B2) as a cofactor.

GSR is an important enzyme in the body's antioxidant defense system as it protects cells from oxidative damage by free radicals. Problems with its function may explain why some people struggle when taking glutathione. One must have sufficient GSR function before supplementing with glutathione or they will simply increase oxidized glutathione. Oxidized glutathione will damage cells via a process called glutathionylation.

Dirties your GSR gene

Environment: Identify and avoid heavy metals, especially arsenic exposures from treated wood products and air pollution sources.

Lifestyle: Alcohol

Food: Avoid foods and drinks high in arsenic such as rice and some tap water, especially from wells.

Supplements and Medications: Glutathione supplementation without sufficient levels of B2 may increase levels of oxidized glutathione which causes poor response to the glutathione.

Cleans your GSR gene

Lifestyle: Yoga has been shown to increase GSR activity.

Food: Vitamin B2 rich, garlic, cinnamon, kimchi

Supplements and Medications: It is important to optimize vitamin B2 prior to using glutathione otherwise it may be unable to be recycled back to active glutathione and remain in its inactive, oxidized form. Consider garlic extracts and powder, quercetin, spirulina, *Bacopa monneri* (brahmi), *Panax ginseng*, *Lippia citriodora* (lemon verbena), *Rhodiola rosea*, *Cinnamomi cassiae*, *Hippophae rhamnoides* (sea buckthorn), liposomal glutathione or S-acetyl glutathione.

Notable variation:

SNP: **GSR -386C>A rs1002149 (+/-, TG)**
This GT variant may upregulate GSR gene activity. Therefore, it is important to ensure adequate B2 status.

THE G6PD GENE

The G6PD (glucose-6-phosphate dehydrogenase) gene expresses an enzyme which recycles NADP+ back to NADPH.

NADPH is, in turn, a vital cofactor for the GSR (glutathione reductase) enzyme to recycle damaged or oxidized glutathione back to its healthy, active form.

Glutathione is an important antioxidant but when it's oxidized, it can damage other proteins via a process called glutathionylation. Therefore, G6PD plays an integral role in supporting the body's antioxidant defense system.

G6PD deficiency impairs intracellular calcium transport and impacts all the major enzymes dependent on NADPH: antioxidant enzymes such as GSR and catalase; nitric oxide synthase, dihydrofolate reductase, NADPH oxidase, cytochrome p450 enzymes, oxidoreductases, and lipid synthesis enzymes such as HMG CoA reductase.

The G6PD protein is located on the X chromosome, therefore males only inherit one allele and females have inherently higher activity as a result of two X chromosomes.

Over 400 variants are known to cause mild to severe G6PD deficiency and this test does not investigate all possible variants for the condition.

💩 Dirties your G6PD gene

Environment: Aluminum, polycyclic aromatic hydrocarbons (PAH), oxidative stress

Lifestyle: Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections. Starvation, fasting, blood sugar dysregulation can all stress G6PD.

Food: Fava beans, omega-6 fats

Supplements and Medications: Acetaminophen (Tylenol), aspirin, high dose vitamin C

Cleans your G6PD gene

Lifestyle: Engage in moderate exercise, especially if supported concurrently with below supplements.

Food: Choose a high complex carbohydrate, low fat diet with mono-unsaturated fats, vitamin D and E rich foods.

Supplements and Medications: Optimize Vitamin D, vitamin E, omega-3: alpha-linolenic acid (ALA) and docosahexaenoic acid (DHA).

Notable variation:

StrateGene does not identify variations in G6PD, so we are presenting this gene's information to you because it is so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

THE GSTA1 GENE

The GSTA1 (glutathione S-transferase alpha 1) gene expresses an enzyme of the alpha class glutathione S-transferase (GST) which functions to add glutathione to target electrophilic compounds, including carcinogens, therapeutic drugs, environmental chemicals and products of oxidative stress.

The alpha class of the GST enzymes (GSTA1 being one of them) exhibit glutathione peroxidase activity neutralizing reactive oxygen species and the products of peroxidation.

Found mainly in liver and kidney, the GSTA1 enzyme also metabolizes bilirubin and certain anti-cancer drugs in the liver.

Dirties your GSTA1 gene

Environment: Pay attention to indoor air quality of home, school or workplace, especially if history of water damage and potential for mold and mycotoxin exposures. Avoid xenobiotics of all types such as plasticizers, polyaromatic hydrocarbons (PAH), pesticides and smoke. Cooking itself, especially without proper ventilation or with low smoke point oils like walnut, flaxseed, wheatgerm can dramatically reduce indoor air quality.

Lifestyle: Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections. Limit use of synthetic chemicals in everyday life.

Food: Limit fatty meats and animal fats such as butter or lard which concentrate dioxins; nitrosamines found in cured meats, cooked bacon, beer, some cheeses, non-fat dry milk.

Supplements and Medications: Avoid acetaminophen (Tylenol), NSAIDs. Consider *Saccharomyces boulardii* while taking antibiotics and probiotics afterwards.

Notable variation:

SNP: **GSTA1 C-69T rs3957357 (+/-, AG)**

The AG variant showed a 50% decrease in expression and activity compared to wild type in vitro. The issue of speed/rate of GSH conjugation of compounds by GSTA1 is somewhat moot, as some end products are less toxic while others are more toxic.

Cleans your GSTA1 gene

Environment: Use water filters and air filters, especially choosing the 'Recirculation of Air' option for in your car versus the "Outside Air" option that allows in vehicle exhaust while driving. Choose high smoke point oils such as avocado oil or ghee, cook in a well-ventilated area and use the extractor hood.

Lifestyle: Choose non-toxic products for household and bodycare use.

Food:

- Follow a whole foods plant-based diet rich in fiber, cruciferous vegetables, garlic, onions, soy, lycopene, selenium, vitamin C, coumarins.
- Consider whey protein powder for glutathione support.
- If you do choose to eat meat, purchase organic, free range meat and utilize cooking methods that employ lower, indirect heat such as braising or stewing which decrease polyaromatic hydrocarbon (PAH) formation.
- Polyaromatic hydrocarbons (PAH) from chargrilling meat may also be reduced by marinating meats for 4 hours prior to grilling in beer, vinegar or tea (both green or black) based sauces including lemon, onions, garlic, or alternatively: spraying meat with culinary vinegar prior to grilling. Polyaromatic hydrocarbon formation was decreased in a study by almost 80% using white wine vinegar, 66% by red wine and cider vinegar, and 55% by raspberry vinegar.

Supplements and Medications: Spirulina, selenium, liposomal glutathione, S-acetyl glutathione, N-acetylcysteine (NAC), vitamin C, probiotics, EGCG from green tea, *Cinnamomi cassiae* and *Rhodiola rosea*

THE GSTO GENE

The GSTO1 and 2 (glutathione S-transferase omega 1 and 2) genes express enzymes of the omega class glutathione S-transferase (GST) which catalyzes thioltransferase, ascorbate, and S-phenacyl glutathione reductase reactions.

The two genes are also involved in the detoxification steps of arsenic biotransformation and are thought to activate interleukin-1b.

GSTO2 possesses twice the antioxidant activity of GSTO1.

Dirties your GSTO gene

Environment: Pay attention to indoor air quality of home, school or workplace, especially if history of water damage and potential for mold exposures, specifically ochratoxins. Xenobiotics of all types such as plasticizers, polyaromatic hydrocarbons (PAH), pesticides and smoke. Couples considering conception should avoid any and all sources of arsenic or cadmium and detox any arsenic and other detected heavy metal burden well in advance of conception.

Lifestyle: Persistent organochlorine pollutants (PCB, DDT), bisphenol A (BPA), plastics, compounds in some antibacterial soaps and dioxin-like compounds can all have long-term inhibitory effects on the glucuronidation capacity of the liver.

Food: Limit fatty meats and animal fats such as butter or lard which concentrate dioxins; nitrosamines found in cured meats, cooked bacon, beer, some cheeses, non-fat dry milk.

Notable variation:

SNP: **GSTO1 -2200G>A rs11509438 (-/-, GG)**
The GG wild type has 150% higher activity when compared with the minor AA variant enzyme in vitro. This translates to potentially lower levels of compounds that contribute to neuro and cardiovascular inflammation. The efficiency of biotransformation of arsenic into less toxic metabolites is still unknown.

SNP: **GSTO1 C419A rs4925 (+/+, AA)**
This AA variant had 40% lower activity when compared with wild type in vitro. This translates to higher levels of compounds that contribute to neuro and cardiovascular inflammation. Thiol transferase reactions appear unchanged compared to wild type. The efficiency of arsenic detoxification appears to be improved; although limited protective evidence exists now, this may equate to lower levels of compounds that initiate some cancers.

SNP: **GSTO2 A424G rs156697 (-/-, GG)**
This wild type GG allele may exhibit lower enzyme expression compared to AA and appears to be the riskier genotype. It is included here for investigational purposes in anticipation of future research that can better characterize its impact.

Cleans your GSTO gene

Environment: Use water filters and air filters, especially choosing the 'Recirculation of Air' option for in your car versus the "Outside Air" option that allows in vehicle exhaust while driving. Be sure to use high smoke point oils such as avocado oil or ghee, cook in a well-ventilated area and use the extractor hood.

Lifestyle: Choose non-toxic products for household and bodycare use.

Food:

- Follow a whole foods plant-based diet rich in fiber, cruciferous vegetables, garlic, onions, soy, lycopene; selenium, vitamin C and coumarin rich foods, whey protein powder.
- Choose meat cooking methods that employ lower, indirect heat such as braising or stewing which decrease polyaromatic hydrocarbon (PAH) formation.
- Polyaromatic hydrocarbons from chargrilling meat may also be reduced by marinating meats for 4 hours prior to grilling in beer, vinegar or tea (both green or black) based sauces including lemon, onions, garlic, or alternatively: spraying meat with culinary vinegar prior to grilling. Polyaromatic hydrocarbon formation was decreased by almost 80% using white wine vinegar, 66% by red wine and cider vinegar, and 55% by raspberry vinegar.
- Be sure to use high smoke point oils such as avocado oil or ghee, cook in a well-ventilated area and use the extractor hood.

Supplements and Medications: Spirulina, sulforaphane, selenium, liposomal glutathione, S-acetyl glutathione, N-acetylcysteine, vitamin C, probiotics, EGCG, *Cinnamomi cassiae* and *Rhodiola rosea*

THE GSTP1 GENE

The GSTP1 (glutathione S-transferase pi 1) gene expresses an enzyme of the pi class glutathione S-transferase (GST) which detoxifies polyaromatic hydrocarbons (PAH) using glutathione.

The GSTP1 gene is also a tumor suppressor gene and is implicated in a large variety of detoxification and metabolism reactions which prevents cells from genome damage and cancer initiation.

Dirties your GSTP1 gene

Environment: Identify and treat heavy metal burden especially aluminum, mercury. Pay attention to indoor air quality of home, school or workplace, especially if history of water damage and potential for mold exposures. Minimize exposure to xenobiotics of all types such as plasticizers, polyaromatic hydrocarbons (PAH), pesticides and smoke.

Lifestyle: Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections including viral hepatitis. Infrequent or minimal sweating may lead to increased chemical burden as many compounds sweat out via the skin: our largest detoxification organ. Limit use of synthetic chemicals in everyday life.

Food: Limit fatty meats and animal fats such as butter or lard which concentrate dioxins. Avoid the Dirty Dozen as explained by Environmental Working Group. Consider *Saccharomyces boulardii* while taking antibiotics and probiotics afterwards.

Supplements and Medications: Acetaminophen (Tylenol), non-steroidal anti-inflammatory drugs (NSAIDs)

Notable variation:

SNP: **GSTP1 GSTP1*B rs1695 (-/-, AA)**

The AA wild type functional effect varies depending on the substrate. The AA active site may better accommodate more bulky compounds but has a smaller range of substrates it can conjugate. Relative to GG individuals, AA individuals have decreased ability to conjugate polyaromatic hydrocarbons (PAH), similar ability to conjugate the pesticide atrazine but more ability to conjugate the cancer drug busulfan or some benzene derivatives. A allele carriers may be at increased risk for inflammation from passive tobacco smoke, asbestos; conflicting evidence for polyaromatic hydrocarbons (PAH), ozone

SNP: **GSTP1 A114V rs1138272 (-/-, CC)**

This CC wild type seems more efficient compared to variant alleles at overall detoxification of most, but not all compounds that require conjugation with glutathione such as polyaromatic hydrocarbons (PAH). Increased activity is due to higher expression and improved substrate access to the catalytic site.

Cleans your GSTP1 gene

Environment: Use water filters and air filters, especially choosing the 'Recirculation of Air' option for in your car versus the "Outside Air" option that allows in vehicle exhaust while driving. Use an extractor hood while cooking and high-smoke point oils like ghee or avocado oil.

Lifestyle: Choose non-toxic products for household and bodycare use.

Food:

- Consume organic fruits, organic vegetables, organic grain and organic dairy products whenever possible. Prioritize your food dollars by knowing the Clean 15 as explained by Environmental Working Group .
- Whole foods plant-based diet rich in fiber, cruciferous vegetables, garlic, onions, soy, lycopene; selenium, vitamin C and coumarin rich foods, whey protein powder are all good choices.
- Choose meat cooking methods that employ lower, indirect heat such as braising or stewing which decrease polyaromatic hydrocarbon (PAH) formation. Polyaromatic hydrocarbons from chargrilling meat may also be reduced by marinating meats for 4 hours prior to grilling in beer, vinegar or tea (both green or black) based sauces including lemon, onions, garlic, or alternatively: spraying meat with culinary vinegar prior to grilling. Polyaromatic hydrocarbon formation was decreased by almost 80% using white wine vinegar, 66% by red wine and cider vinegar, and 55% by raspberry vinegar.

Supplements and Medications: Spirulina, selenium, liposomal glutathione, S-acetyl glutathione, N-acetylcysteine (NAC), vitamin C, probiotics, EGCG from green tea, sulforaphane, *Cinnamomi cassiae* and *Rhodiola rosea*

THE NOX GENE

The NOX (NADPH oxidase) genes express enzymes which catalyze the production of a superoxide free radical (O2-). NOX2 is composed of 2 cytochrome subunits coded by the genes CYBA and CYBB and uses FAD (derived from riboflavin, B2), NADPH (derived from niacin, B3) and heme as cofactors.

NOX is found in two places: one in white blood cells (neutrophilic) and the other in vascular cells. Neutrophilic NOX produces superoxide almost instantaneously, whereas the vascular version produces superoxide in minutes to hours.

The enzyme becomes rapidly activated in the presence of bacteria and other pathogens and generates superoxide in an attempt to kill and eliminate them. However, persistent stimulation of NOX2 may lead to excessive production of superoxide in vascular cells, increasing susceptibility to cardiovascular disease.

This is yet another reason why it's so important to identify infections of any type (bacterial, viral, mold, parasites) in every part of the body (nose, mouth, ears, sinuses, bones, blood, digestive system to name a few).

Dirties your NOX gene

Environment:

- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage as heme is the required cofactor for this enzyme.
- Also, many parasites and gram negative bacteria need heme to reproduce and cause infection. These pathogens must synthesize their own heme or steal heme from the host. Thus, untreated chronic parasite or bacterial infections may create a heme deficiency. (Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.)
- Be mindful of tick infested areas as they increase the risk of Lyme disease.
- Pay attention to indoor air quality of home, school or workplace, especially if history of water damage and potential for mold exposures. Cooking itself, especially without proper ventilation or with low smoke point oils like walnut, flaxseed, wheatgerm can dramatically reduce indoor air quality.

Notable variation:

SNP: **NOX -930G>A rs9932581 (-/-, CC)**

This CC variant exhibits higher enzyme expression in vitro with more generation of reactive oxygen species, especially in response to smoking or obesity. This can increase risk for cardiovascular and other inflammatory diseases, but is protective against pathogenic bacteria and fungi as it results in more oxidative stress needed to fight infection.

Dirties your NOX gene, continued...

Lifestyle:

- Obesity typically causes inflammation and taxes NOX.
- Avoid smoke from incense, woodsmoke, air pollution, vehicle exhaust, cooking with low smoke point oils.
- Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections.

Food: NOX is especially sensitive to damage from the standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium and low in fiber and good quality protein. Especially avoid oxidized omega-6 fatty acids (from rancid, processed or low smoke point cooking oils), saturated fats, microwaved foods containing cholesterol or animal products.

Supplements and Medications: Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your NOX gene

Environment: Use an extractor hood while cooking. Utilize air filtration systems to remove molds, bacteria and viruses and water filtration to remove potential pathogenic bacteria.

Lifestyle: Maintain optimal weight and blood sugars. Nutritional ketosis may be helpful, as can cardiovascular exercise. Stress management techniques are recommended such as meditation, breathing exercises, mindfulness, outdoor time, massage, pet therapy, moderate physical exercise.

Food: When cooking, use high smoke point oils such as ghee or avocado oil. Opt for a whole foods plant based or Mediterranean diet rich in extra virgin olive oil, cold water fish, legumes, nuts, seeds, fruits and vegetables. Choose vitamin A, riboflavin (B2), heme and non-heme iron rich foods. Foods naturally rich in SOD include cabbage, Brussels sprouts, wheat grass, barley grass and broccoli.

Supplements and Medications:

- Optimize riboflavin (B2), niacin (B3), iron, vitamin A and D levels.
- While you need NOX to express during acute infections in order to produce sufficient oxidants to target and kill pathogens, chronically activated NOX will lead to persistent and unwanted oxidative stress. In those in this situation of upregulated NOX unrelated to infection, a SOD supplement may be helpful in neutralization of high oxidant levels, as well as supporting the genes downstream of NOX: CAT and GPX.
- Spirulina, berberine, green tea, resveratrol, curcumin, olive leaf extract, hesperidin and quercetin all have been shown to lower oxidative stress from overactive NOX genes.
- In the scenario of acute infections, antimicrobials and other pro-oxidant therapies such as IV vitamin C, can assist in the elimination of the infection thereby reducing the need for NOX to over-express.

THE SOD2 GENE

The SOD2 gene (mitochondrial superoxide dismutase 2 – also known as MnSOD) expresses an enzyme in the mitochondria that reduces levels of superoxide radicals by converting them into hydrogen peroxide, using manganese (Mn) as a cofactor.

Superoxide radicals are important and useful in the body when present in the right amount. Superoxide then participates in a beneficial purging process known as “programmed cell death” as a burst of superoxide radicals causes death to damaged and worn-out cells. However, an excess of superoxide may cause inflammation resulting in uncontrolled death of healthy cells.

SOD2 enzymes take the very reactive superoxide radicals made by NOX and convert them into slightly less reactive, but still damaging, hydrogen peroxide.

Like superoxide, hydrogen peroxide is also important and useful in the right amount. In the body it is used to kill bacteria, fungi and other pathogens. However, again, in excess, hydrogen peroxide can also cause inflammation and cell damage/death.

The hydrogen peroxide generated by SOD2 is converted to water and oxygen by either GPX or CAT enzymes. Therefore, the balance between these enzymes is crucial in controlling the levels of these highly reactive, yet important compounds.

If SOD2 is working slowly, superoxide levels may build up. This increases the risk of superoxide combining with nitric oxide to generate peroxynitrite, which is another damaging and reactive pro-oxidant.

On the other hand, if SOD2 is working quickly, and doing a good job of reducing superoxide, this may then cause a build-up of hydrogen peroxide. This is especially the case for those with slow GPX1 (present) or slow CAT (unknown) genes who cannot convert the damaging hydrogen peroxide to harmless water fast enough.

An ideal situation is when SOD2 works quickly along with GPX and CAT also functioning well. This demonstrates the importance, again, of how many genes are required to function well, and interact with each other, in order to provide optimal health.

The activity of SOD2 is naturally higher in females by approximately 15%.

Notable variation:

SNP: **SOD2 A16V rs4880 (+/-, AG)**

This AG variant may result in 15-20% higher activity in vivo relative to wild type GG.

Dirties your SOD2 gene

Environment: Work with your healthcare provider to identify and treat any infections: viral, bacterial or fungal; heavy metals or bisphenol A (BPA) burden.

Lifestyle:

- Work with your healthcare provider to identify and treat sleep apnea.
- Extensive exercise or overtraining causes significant inflammation and oxidative stress.
- Limit alcohol.

Food: Avoid the standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium, oxidized inflammatory fats, and low in fiber.

Supplements and Medications: While pro-oxidant therapies such as ozone, IV vitamin C, hyperbaric oxygen therapy (HBOT) are very beneficial for many people, they may exacerbate those with a weakened antioxidant response. If experiencing pain or significant worsening of symptoms with these pro-oxidant therapies, it may be good to evaluate the antioxidant genes such as SOD, CAT, GPX. Be mindful of manganese supplementation. While it is the cofactor, high manganese is proinflammatory and may lead to an exacerbation of symptoms. Do not over supplement with manganese.

Cleans your SOD2 gene

Lifestyle: Physical exercise in moderation. Exercise increases oxidative stress. If post-workout soreness extends beyond 48 hours, then consider reducing intensity, frequency and duration.

Food:

- Choose a low sodium diet of 1,200-1,500 mg sodium/day.
- Focus on sources rich in manganese, vitamin C and sulforaphane such as cruciferous vegetables like broccoli, cabbage, cauliflower, Brussels sprouts and kale
- Opt for a Mediterranean diet rich in extra virgin olive oil, cold water fish, legumes, nuts, seeds, fruits and vegetables or whole food plant-based diet.
- A moderate protein diet of 0.8 grams of protein per kg (2.2 lbs) of body weight per day is recommended. After age 65, moderate protein is associated with reduced mortality suggesting an increased protein intake and the resulting increase in IGF-1 and SOD2 may prove beneficial in older adults.

Cleans your SOD2 gene, continued...

Supplements and Medications:

- Optimize manganese and selenium.
- Consider *Lactobacillus spp.*, melatonin, lutein, pycnogenol, curcumin, resveratrol, carnitine, PQQ (pyrroloquinoline quinone), SOD, carnosine, CoQ10, *Rhodiola rosea*.
- When supporting SOD, it is important to also support downstream enzymes, GPX and CAT, with their cofactors. If you do not, an increase in SOD activity may burden these enzymes leading to excessive hydrogen peroxide (H_2O_2) levels.
- Additional support of GSR is needed to recycle oxidized glutathione back to its active, reduced form.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

THE GPX1 GENE

The GPX1 (glutathione peroxidase 1) gene expresses an enzyme which is responsible for the detoxification of peroxides such as hydrogen peroxide, organic hydroperoxides and lipid hydroperoxides. Selenium is required for the active catalytic site.

There are 8 known isoforms of glutathione peroxidase (GPX 1-8). GPX1 primarily protects against harmful levels of hydrogen peroxide within the cell by transforming it to water.

Dirties your GPX1 gene

Environment: Identify and treat heavy metal burden especially mercury (Hg) and lead (Pb). Avoid excess iron (Fe) which, in the presence of hydrogen peroxide, increases oxidative stress and causes cell damage. Therefore, individuals with familial hemochromatosis (HFE), postmenopausal women and men should identify any unwanted sources of iron in diet such as well water, cookware, supplements. Avoid chlorine found in showers, drinking water, swimming pools, hot tubs; formaldehyde found in carpets, new furniture, cabinets, gas appliances.

Lifestyle: Alcohol

Supplements and Medications: Avoid iron (Fe) if elevated.

Cleans your GPX1 gene

Food: Drink vinegar: one tbsp apple cider vinegar in glass of water before meals. Choose selenium vitamin C rich sources; sulforaphane rich found in cruciferous vegetables such as broccoli, cabbage, cauliflower, Brussels sprouts and kale.

Supplements and Medications: Consider vitamin E, liposomal glutathione, S-acetyl glutathione, cinnamon, curcumin, genistein, ECGC, quercetin, melatonin, resveratrol, spirulina, *Hippophae rhamnoides* (sea buckthorn), *Rhodiola rosea, Cinnamomi cassiae* and *Withania somnifera* (ashwagandha) which help to reduce inflammation.

Optimize selenium, copper and zinc. Copper and especially zinc are shown to inhibit GPX1 activity. This is useful and necessary under conditions of bacterial infection, when adequate levels of copper and especially zinc allow for the immune system to generate sufficient hydrogen peroxide to fight infections. However, avoid over-supplementation. Use the 'pulse method' described in the *Dirty Genes* book.

Estrogen increases GPX activity. If you are a postmenopausal woman: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Notable variation:

SNP: **GPX1 -46C>T rs1800668 (+/-, AG)**

This GA variant has 20% less activity than wild type in vivo. This reduces the capacity of active glutathione to neutralize oxidants such as hydrogen peroxide (H_2O_2)

THE GPX4 GENE

The GPX4 (glutathione peroxidase 4) gene expresses an enzyme which is responsible for the detoxification of phospholipid hydroperoxide, fatty acid hydroperoxide and cholesterol hydroperoxide found in cell membranes and lipoproteins. Selenium is required for the active catalytic site.

There are 8 known isoforms of glutathione peroxidase (GPX 1-8). GPX4 protects against cell death resulting from an iron-triggered accumulation of lipid reactive oxygen species.

Dirties your GPX4 gene

Environment: Avoid smoke from any source: cigarettes, marijuana, incense, woodsmoke, diesel exhaust, smog, cooking fumes. Individuals with familial hemochromatosis (HFE), men and postmenopausal women should identify any unwanted sources of iron in diet such as well water, cookware, supplements. Use air filtration systems that remove combustion products from natural gas fireplaces, cooktops or ranges; formaldehyde sources such as carpets, new furniture, cabinets, gas appliances. Use water filters to remove chlorine sources such from showers, drinking water, swimming pools, hot tubs, baths.

Food: Limit arachidonic acid, avoid rancid omega-6 fats; heating low smoke point oils like walnut, flaxseed, wheatgerm can make them unfit for consumption.

Supplements and Medications: Iron, especially if elevated

Cleans your GPX4 gene

Environment: Use an extractor hood while cooking and high-smoke point oils like ghee or avocado oil.

Food: Opt for whole food plant-based diet, choose selenium rich sources.

Supplements and Medications: Consider selenium. The optimal benefits of supplementation on DNA stability are observed when the serum selenium level reaches between 160> x >120 ng/ml.

Notable variation:

SNP: **GPX4 C718T rs713041 (+/+, TT)**

This TT variant appears to express differently depending on selenium status. Adequate selenium status is important but excess selenium may actually have an adverse effect.

With sufficient selenium, the activity of this TT variant in white blood cells appears to be equivalent to wild type. However, in selenium deficient states, activity of the TT variant falls relative to wild type. However, a more recent study found the opposite effect, perhaps due to larger haplotype effects and/or different cell line utilized.

The TT variant also appears to affect the transcription of other GPX enzymes, with GPX4 TT falling lowest in the hierarchy of enzyme synthesis when selenium is deficient. This effect was observed in women, not men, although not extensively studied or well understood.

THE CAT GENE

The CAT (catalase) gene expresses an enzyme which catalyzes the decomposition of hydrogen peroxide into oxygen and water using NADPH (derived from niacin, B3) and heme as cofactors.

Hydrogen peroxide is a by-product of many normal metabolic processes but can cause harmful oxidative damage to cells and tissues if not neutralized.

The catalase enzyme is therefore important for protecting cells from oxidative damage, and it has one of the highest activities of the antioxidant enzymes. One catalase molecule converts millions of hydrogen peroxide molecules to water and oxygen each second.

Catalase can also use hydrogen peroxide to catalyze the break down of various metabolites and chemicals including formaldehyde, formic acid, phenols, acetaldehyde and alcohols.

💩 Dirties your CAT gene

Environment: Pesticides, pollutants, metals, smoking. Iron overload, individuals with familial hemochromatosis (HFE) or thalassemia. Men and postmenopausal women should identify any unwanted sources of iron in diet such as well water, cookware, supplements.

Lifestyle:

- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage as heme is the required cofactor for this enzyme.
- Also, many parasites and gram negative bacteria need heme to reproduce and cause infection. These pathogens must synthesize their own heme or steal heme from the host. Thus, untreated chronic parasite or bacterial infections may create a heme deficiency. (Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.)
- Individuals with beta-thalassemia may be at increased risk for serious complications due to increased oxidative stress. Therefore, avoid vigorous exercise or overtraining which causes significant inflammation and oxidative stress.

Food: Avoid the standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium, oxidized inflammatory fats, and low in fiber and good quality protein. Individuals with a dirty CAT should seriously consider eating nutritious whole foods.

Supplements and Medications: Iron, especially if elevated

Notable variation:

SNP: **CAT 1167C>T rs769217 (-/-, CC)**
Wild type CC carriers exhibit faster transcription compared to variant carriers and thus have slightly higher catalase levels compared to TT. This may increase susceptibility to pulmonary oxidative damage from ozone and air pollution.

SNP: **CAT -262C>T rs1001179 (+/+, TT)**
The TT variant results in a mild downregulation. Carriers of a T allele may therefore be slightly more prone to systemic oxidative stress damage from pesticides, pollutants, metals, smoking.

Cleans your CAT gene

Lifestyle: Engage in enjoyable exercise, especially moderate-intensity continuous training.

Food: Choose beta-carotene, niacin (B3), heme and non-heme iron, omega-3 fatty acid rich sources. Following a diet rich in fruit and vegetables with additions of vinegar, garlic, cinnamon, black tea can support catalase.

Supplements and Medications: Consider niacin (B3), iron, appropriate probiotics, beta-carotene, omega-3 fatty acids, inositol, melatonin, resveratrol, carnitine, catalase, liposomal glutathione, s-acetyl-glutathione, PQQ (pyrroloquinoline quinone), carnosine, *Rhodiola rosea*, *Cinnamomi cassiae*, *Hippophae rhamnoides* (sea buckthorn).

THE MPO GENE

The MPO (myeloperoxidase) gene expresses a heme-containing enzyme that generates hypochlorous acid (HOCl) from chloride (Cl-) and hydrogen peroxide (H_2O_2).

MPO can also utilize hydrogen peroxide to generate tyrosyl radicals from tyrosine.

Hypochlorous acid and tyrosyl radicals are cytotoxic (damaging to the cell), but in the body's immune system, white blood cells utilize MPO to generate these toxic compounds to kill invading bacteria, viruses, and fungi.

These compounds may then also cause tissue damage and inflammation in the host tissues and have been linked to various inflammatory diseases. However, recent studies have demonstrated that MPO deficiency actually results in exaggeration of the inflammatory response. Therefore, despite the potential "collateral damage" at sites of inflammation, MPO is still an important component of the body's defense and repair system.

MPO requires calcium and heme as cofactors.

Dirties your MPO gene

Environment: Avoid excess copper which inhibits MPO activity; as well as pesticides. Avoid the Dirty Dozen as explained by Environmental Working Group.

Lifestyle:

- Identify and treat inflammation.
- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage as heme is the required cofactor for this enzyme.
- Also, many parasites and gram negative bacteria need heme to reproduce and cause infection. These pathogens must synthesize their own heme or steal heme from the host. Thus, untreated chronic parasite or bacterial infections may create a heme deficiency. (Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.)

Supplements and Medications: Avoid acetaminophen (Tylenol), long term use of proton pump inhibitors (Prilosec, Prevacid, Nexium).

Notable variation:

SNP: **MPO 2036A>G rs2243828 (-/-, AA)**

This AA wild type variant may have higher MPO mRNA levels compared to GG/AG. Since the products of MPO activity can be cytotoxic, AA wild types may have increased risk of inflammation and related diseases due to higher production of reactive oxygen species as compared to GG or AG, but more protection against pathogens like H. pylori.

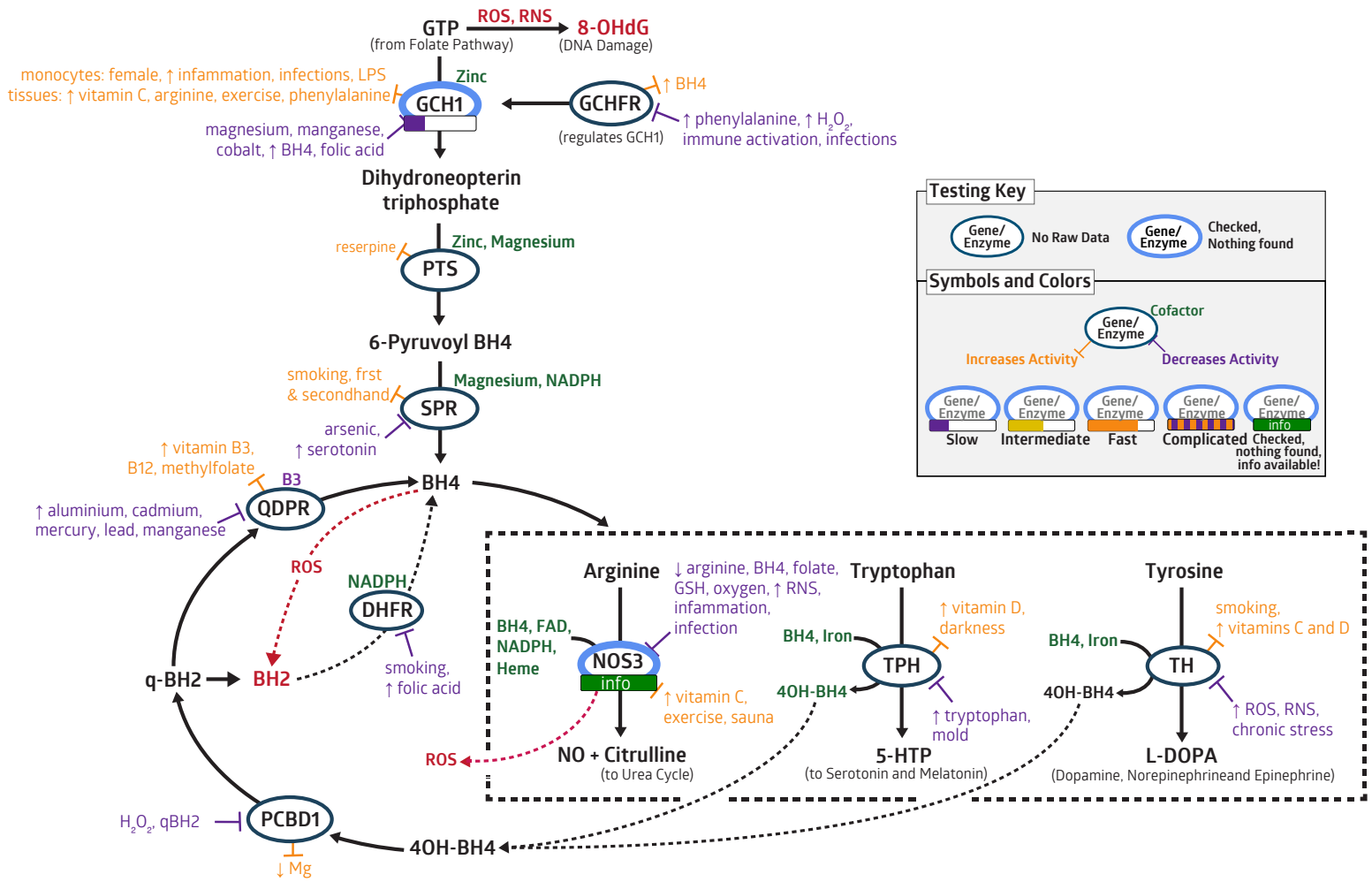
Note: The functional variant rs2333227 is being replaced by the proxy rs2243828 due an inability to confidently determine alleles for rs2333227. See the FAQ for more information."

Cleans your MPO gene

Food: Choose calcium, heme-iron, tyrosine, quercetin rich foods. Consume organic fruits, organic vegetables, organic grain and organic dairy products whenever possible. Prioritize your food dollars by knowing the Clean 15 as explained by Environmental Working Group.

Supplements and Medications: Consider calcium, iron if determined to be iron deficient, tyrosine, quercetin, melatonin, curcumin, EGCG from green tea, *Boswellia spp.* (frankincense), resveratrol.

Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.


GTP
(from Folate Pathway)
ROS, RNS
8-OHdG
(DNA Damage)
monocytes: female, ↑ infammation, infections, LPS
tissues: ↑ vitamin C, arginine, exercise, phenylalanine
Zinc
GCH1
magnesium, manganese, cobalt, ↑ BH4, folic acid
GCHFR
(regulates GCH1)
↑ BH4
↑ phenylalanine, ↑ H2O2, immune activation, infections
Dihydroneopterin triphosphate
reserpine
Zinc, Magnesium
PTS
6-Pyruvoyl BH4
smoking, frst & secondhand
Magnesium, NADPH
SPR
arsenic, ↑ serotonin
↑ vitamin B3, B12, methylfolate
B3
BH4
↑ aluminium, cadmium, mercury, lead, manganese
QDPR
ROS
NADPH
DHFR
smoking, ↑ folic acid
q-BH2
BH2
Arginine
↓ arginine, BH4, folate, GSH, oxygen, ↑ RNS, infammation, infection
BH4, FAD, NADPH, Heme
NOS3
info
↑ vitamin C, exercise, sauna
ROS
NO + Citrulline
(to Urea Cycle)
Tryptophan
↑ vitamin D, darkness
BH4, Iron
TPH
4OH-BH4
↑ tryptophan, mold
5-HTP
(to Serotonin and Melatonin)
Tyrosine
smoking, ↑ vitamins C and D
BH4, Iron
TH
4OH-BH4
↑ ROS, RNS, chronic stress
L-DOPA
(Dopamine, Norepinephrineand Epinephrine)
H2O2, qBH2
PCBD1
↓ Mg
4OH-BH4
Testing Key
Gene/ Enzyme
No Raw Data
Checked, Nothing found
Symbols and Colors
Cofactor
Increases Activity
Decreases Activity
Slow
Intermediate
Fast
Complicated
Checked, nothing found, info available!

THE GCH1 GENE

The GCH1 (GTP cyclohydrolase 1) gene expresses an enzyme which catalyzes the first and rate-limiting step in the biosynthesis of BH4 (tetrahydrobiopterin or biopterin): the conversion of guanosine triphosphate (GTP) to dihydroneopterin triphosphate using zinc as a cofactor.

BH4 is an essential co-factor, directly or indirectly, for the production of serotonin, melatonin, dopamine, norepinephrine, epinephrine and nitric oxide. If synthesis of BH4 is reduced, this negatively affects the important processes of neurotransmitter formation, cardiovascular and endothelial function, immune response and reduces pain sensitivity. Excessive formation of BH4, on the other hand, may lead to increased pain sensitivity.

Optimizing BH4 levels is, however, difficult: Under conditions of oxidative stress, guanosine triphosphate (GTP), the substrate for GCH1, becomes damaged by reactive oxygen and nitrogen species (ROS and RNS) and is converted to 8-hydroxy-2'-deoxyguanosine (8-OHdG), a biomarker for oxidative stress on lab tests.

This means that in the presence of oxidative stress, the GCH1 gene is lacking GTP for which to synthesize BH4. (This is similar to the 'Tryptophan Steal' as explained in the Serotonin Pathway.)

Even if GCH1 is upregulated and there is enough GTP available, BH4 still may not be synthesized because, especially during times of immune activation, GCH1's product dihydroneopterin triphosphate may get diverted to become neopterin. Neopterin is then used by the immune system to fight infections via the cell-mediated immune response.

In other words, during times of infection, BH4 synthesis may be reduced due to increased neopterin synthesis.

An additional factor that may impact BH4 synthesis, is that GCHFR acts to regulate expression of GCH1, and if the GCHFR gene is stimulated, it slows the expression of GCH1.

Finally, one has to be aware of the important role that recycling of oxidized BH4 plays in keeping BH4 at a sufficient level.

This recycling process is performed by a few genes and one is DHFR (discussed in the Folate Pathway). If the DHFR gene is slowed by synthetic folic acid and there is decreased synthesis of BH4 via the GCH1 enzyme, there is going to be a significant shortage of BH4. This will lead to significant neurological and cardiovascular dysfunction.

Once again, we see the importance of knowing the whole picture and how genes work together, and why they do so, versus just knowing what SNPs you have.

Notable variation:

A GCH1 Slow Haplotype

This 3-allele haplotype showed reduced BH4 levels compared to wild type in an in vitro model. In a cohort of European descent with cardiovascular disease, this variant haplotype exhibited 40% reduced flow mediated vasodilation in response to experimental inflammatory stimulus reflective of lower BH4 levels compared to wild type. Another cohort showed 75% less BH4 production when stimulated by an inflammatory chemical.

Gene	rsID	Alias	Variant Allele	Call
GCH1	rs8007267	G-9610A	T	TC
GCH1	rs3783641	A8900T	A	AT
GCH1	rs10483639	G4279C	C	CG

Dirties your GCH1 gene

Lifestyle:

- Inflammation, smoking and elevated blood sugars are especially serious for this gene and should be addressed as a first priority.
- Autoimmune disease (such as rheumatoid arthritis) can also affect this gene.
- Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections.

Food: Avoid processed foods as they contain synthetic folic acid, as well as high glycemic foods such as high-sugar beverages, cakes/cookies, white bread/rice/pasta, french fries, candies, dried fruit.

Supplements and Medications:

- Avoid synthetic folic acid, glucocorticoids (hydrocortisone, prednisone).
- Oxidative therapies such as IV vitamin C, ozone and hyperbaric oxygen therapy (HBOT) may contribute to high reactive oxygen and nitrogen species (ROS and RNS) thereby diverting GTP substrate to DNA damage.
- Many medications interact with this enzyme. Consult your healthcare provider or pharmacist.

Cleans your GCH1 gene

Lifestyle: Engage in far-infrared sauna use, moderate exercise and healthy sun exposure (vitamin D) to support healthy blood sugar regulation.

Food: Foods rich in arginine, vitamin C, zinc, folate, and phenylalanine.

Supplements and Medications:

- Enhanced levels of phenylalanine induce the transcription of GCH1. Thus, phenylalanine enhances the BH4 concentration not only through reversing the negative feedback inhibition of GCH1 but also through inducing synthesis.
- Consider zinc and vitamin C, antioxidant support.
- Folate as folinic acid is important to support production of guanosine.
- Methylfolate (L-5-MTHF) is needed if homocysteine is elevated.
- Use antioxidants such as PQQ (pyrroloquinoline quinone), liposomal glutathione, S-acetyl glutathione, carnosine, SOD (superoxide dismutase) to help quench reactive oxidative species (ROS) and reactive nitrogen species (RNS) so GTP substrate can engage with the GCH1 enzyme versus getting damaged and being unable to bind to the enzyme.
- Chromium to support blood sugar along with acetyl-L-carnitine and vitamin D.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

THE NOS3 GENE

The NOS3 (nitric oxide synthase 3, endothelial aka eNOS) gene expresses an enzyme that regulates production of nitric oxide (NO) in endothelial blood vessel cells using cofactors: tetrahydrobiopterin (BH4), heme, FAD (derived from riboflavin, B2) and NADPH (derived from niacin, B3).

Nitric oxide, a vital gasotransmitter molecule, inhibits platelet aggregation, results in relaxation and inhibition of cell proliferation of endothelial smooth muscle, stimulates angiogenesis, acts as an anti-inflammatory molecule, and prevents oxidative damage.

NOS3 is very important for pregnancy, cardiovascular health and general blood flow. NOS3 can generate a significant amount of superoxide, a reactive oxygen species which is very damaging to BH4 recycling.

If NOS3 lacks any of its cofactors or is inhibited in any way (low glutathione, high homocysteine, low arginine), it may utilize arginine to synthesize harmful superoxide instead of useful nitric oxide. This is called NOS uncoupling. This explains why there can be resistance to nitroglycerin and supplemental arginine. Read the NOS3 chapter in *Dirty Genes* to learn more about this important gene.

💩 Dirties your NOS3 gene

Environment: Avoid carbon monoxide, due to less oxygen availability; and smoking, due to depletion of glutathione.

Lifestyle:

- Mouth breathing does not produce nitric oxide while nose breathing does. Thus, mouth breathing is damaging as it prevents the normal nitric oxide production from nasal breathing and contributes to hypoxia. Snoring is a sign of impaired breathing while sleeping. Check for sleep apnea or other causes.
- Elevated blood sugars and inflammation are especially serious for this gene and should be addressed as a first priority.
- People with heme synthesis issues such as sideroblastic anemia or one of the many porphyria disorders may be at disadvantage as heme is the required cofactor for this enzyme.
- Many parasites and gram negative bacteria may steal the iron-containing cofactor, heme, to reproduce and cause infection. Thus, untreated chronic parasite or bacterial infections may create a heme deficiency. Work with your healthcare provider to identify and treat intestinal dysbiosis or other infections rather than just correcting a heme deficiency.

Notable variation:

While no notable variation was found, we are presenting this gene's information to you because it's so important. Remember, lifestyle, food, environment and nutrients play a significant role in genetic expression — often significantly more than a genetic variation.

Dirties your NOS3 gene, continued...

Food: Avoid saturated animal fats and standard American diet (SAD) which is of poor nutritional value: high in processed carbohydrates, sodium, oxidized inflammatory fats, and low in fiber and good quality protein. While this may seem obvious, it's incredibly important to consume nutritious foods if one has a dirty NOS3. Foods which slow MTHFR (Folate Pathway) and GST/GPX (Glutathione Pathway) will also slow NOS3.

Supplements and Medications: Consider *Saccharomyces boulardii* while taking antibiotics and probiotics afterwards. High amounts of arginine or nitroglycerin may deplete other cofactors thereby contributing to NOS uncoupling.

Cleans your NOS3 gene

Environment: Limit exposure to synthetic chemicals as NOS3 is sensitive to environmental contaminants. Indoor and outdoor air quality is a big issue. Use an extractor hood while cooking and high-smoke point oils like ghee or avocado oil. Use air filters in your home and especially in your car, choosing the 'Recirculation of Air' option versus the "Outside Air" option that allows in vehicle exhaust while driving.

Lifestyle: Engage in regular thermal therapy such as: hot yoga, steam rooms, hot baths, far-infrared sauna. Breathe through the nose. Exercise in an environment with minimal pollution. Do not exercise during heavy traffic hours or near busy streets. Ideally, exercise out in nature or indoors with filtered air. Track sleep quality with a device such as an Oura Ring or have your health professional evaluate you for sleep apnea.

Food:

- Choose arginine, riboflavin (B2), folate (B9), vitamin C, nitrate and iron/heme-iron rich sources.
- Opt for a Mediterranean diet rich in extra virgin olive oil, cold water fish, legumes, nuts, seeds, fruits and vegetables.
- Drink strong *Hibiscus sabdariffa* tea. Take apple cider vinegar: one tablespoon in glass of water before meals 2x/day.
- Keep nitrogen balance in order as excessive protein intake may drive up homocysteine. High homocysteine will dirty NOS3 significantly.
- Cruciferous vegetables are important to support production of glutathione which is needed to keep NOS3 cofactor, BH4, undamaged. If BH4 is damaged, the NOS3 enzyme falters and symptoms may occur.

Cleans your NOS3 gene, continued...

Supplements and Medications:

- Consider appropriate amounts of B2, B3, probiotics, melatonin, vitamin C, flavonoids, artichoke leaf extracts and artichoke flavonoids, resveratrol, PQQ (pyrroloquinoline quinone), liposomal glutathione, S-acetyl glutathione, arginine, citrulline, aspirin.
- Postmenopausal women only: Discuss with your healthcare provider the prescription use of bioidentical estrogens (and progesterone if intact uterus), if you are under 55 and within 4 years of the onset of menopause, and if there are other indications for its use.

Histamine

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
HRH1	rs901865	TC		T	-17T>C	+/-
HRH4	rs11662595	AA		G	249A>G	-/-
DAO (AOC1)	rs2052129	TT		T	-691G>T	+/+
DAO (AOC1)	rs10156191	TT		T	47C>T	+/+
HNMT	rs11558538	CC		T	C314T	-/-
NAT2	rs1801279	GG		A		-/-
MAOA	rs6323	TT		G	T941G	-/-
MAOA	rs1137070	CC		T	1410T>C	-/-
MAOB	rs1799836	TT		C	-36A>G	-/-
MAOB	rs2311013	TT		A	1155T>A	-/-
MAOB	rs5905512	AA		A	15106T>C	+/+
ALDH1B1	rs2228093	TC		T	ALDH1B1*2	+/-
ALDH2	rs671	GG		A	ALDH2*2	-/-
ALDH2	rs737280	CC		C	699T>C	+/+

• **A NAT2 Fast Haplotype Found**

-/- variant allele not present; +/- heterozygous genotype; +/+ homozygous genotype; +/+* hemizygous genotype (male X); = much slower; = slower; = intermediate speed; = faster; = much faster; = contextual; = unknown

Dopamine

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
TH	rs2070762	AG		G	127T>C	+/-
TH	rs10770141	GG		A	C-824T	-/-
MAOA	rs6323	TT		G	T941G	-/-
MAOA	rs1137070	CC		T	1410T>C	-/-
MAOB	rs1799836	TT		C	-36A>G	-/-
MAOB	rs2311013	TT		A	1155T>A	-/-
MAOB	rs5905512	AA		A	15106T>C	+/+
ALDH2	rs671	GG		A	ALDH2*2	-/-
ALDH2	rs737280	CC		C	699T>C	+/+
SLC18A1	rs1390938	AG		A	C407T	+/-
DRD2	rs1800497	AG		A	Taq1A	+/-
DRD2	rs12364283	AA		G	-1189T>C	-/-
DRD2	rs1076560	AC		A	-83G>T	+/-
SLC6A3	rs6347	TC		C	1215A>G	+/-
DBH	rs1611115	CC		T	-1021C>T	-/-
SLC6A2	rs2242446	TT		C	-182T>C	-/-
SLC6A2	rs5569	GG		A	G1287A	-/-
ADRB1	rs1801253	CC		G	1165G>C	-/-
ADRB2	rs1042713	AA		A	5285A>G	+/+
ADRB2	rs1800888	CC		T	491C>T	-/-
ADRB2	rs1042714	CC		G	79C>G	-/-
ADRB3	rs4994	AA		G	190T>C	-/-

• **An Intermediate COMT Haplotype Found**

Serotonin

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
IDO2	rs10109853	TC	much slower	T	R248W	+/-
TPH1	rs1799913	GG		T	A779C	-/-
TPH2	rs4570625	GG	much slower	T	G-703T	-/-
SLC18A1	rs1390938	AG	much faster	A	C407T	+/-
HTR2A	rs6311	TC	intermediate speed	T	G-1438A	+/-
HTR2C	rs3813929	TT	much faster	T	C759T	+/+
HTR3A	rs1062613	CC	much slower	T	C178T	-/-
HTR3B	rs1176744	AA	much slower	C	A386C	-/-
MAOA	rs6323	TT	much slower	G	T941G	-/-
MAOA	rs1137070	CC		T	1410T>C	-/-
MAOB	rs1799836	TT	contextual	C	-36A>G	-/-
MAOB	rs2311013	TT		A	1155T>A	-/-
MAOB	rs5905512	AA	unknown	A	15106T>C	+/+
ADH1B	rs1229984	CC		T	ADH1B*2	-/-
ALDH2	rs671	GG		A	ALDH2*2	-/-
ALDH2	rs737280	CC	much slower	C	699T>C	+/+
MTNR1B	rs10830963	CC		G	10922C>G	-/-
CYP1A2	rs762551	AC	contextual	C	-163C>A	+/-
CYP1B1	rs1800440	TT	much faster	C	CYP1B1*4	-/-

• **A less common UGT1A6 Haplotype Found**

Folate

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
SLC19A1	rs1051266	TC	much slower	T	G80A	+/-
MTHFD1	rs2236225	AG	slower	A	G1958A	+/-
MTHFR	rs1801133	AA	much slower	A	C677T	+/+
MTHFR	rs1801131	TT		G	A1298C	-/-
FTCD	rs61735836	CC		T	C301T	-/-

-/- variant allele not present; +/- heterozygous genotype; +/+ homozygous genotype; +/+* hemizygous genotype (male X); much slower; slower; intermediate speed; faster; much faster; contextual; unknown

SAM

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
MTR	rs1805087	AG		G	A2756G	+/-
MTRR	rs1532268	TC		T	C524T	+/-
MTRR	rs1801394	GG		G	G66A	+/+
TCN1	rs34324219	CC		A	901G>T	-/-
TCN2	rs526934	AG		G		+/-
TCN2	rs1801198	CC		G	c.776G>C	-/-
TCN2	rs9606756	AA		G	67A>G	-/-
MAT1A	rs72558181	CC		T	791G>A	-/-
PEMT	rs7946	TT		T	G5465A	+/+
ALDH7A1	rs13182402	AA		G	395T>C	-/-
BHMT	rs3733890	AG		A	716G>A	+/-
DMGDH	rs121908331	TT		C	326A>G	-/-
ADA	rs73598374	NA		T	G22A	NA
ADORA2A	rs2236624	CC		T		-/-
PON1	rs662	TT		T	575A>G	+/+
PON1	rs854560	TT		T	L55M	+/+
PON2	rs7493	GG		C	896C>G	-/-

• **A PON1 575A>G/L55M Haplotype Found**

-/- variant allele not present; +/- heterozygous genotype; +/+ homozygous genotype; +/+* hemizygous genotype (male X); = much slower; = slower; = intermediate speed; = faster; = much faster; = contextual; = unknown

Glutathione

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
CBS	rs121964962	CC		T	919G>A	-/-
CBS	rs121964970	CC		T	V168M	-/-
CBS	rs398123151	GG		A	R336C	-/-
CBS	rs28934891	CC		T	D444N	-/-
CBS	rs4920037	GG		A		-/-
CBS	rs234706	GG		A	C699T	-/-
CTH	rs28941785	CC		T	200C>T	-/-
CTH	rs28941786	NA		G	718C>G	NA
GSR	rs1002149	TG		T	-386C>A	+/-
GSTA1	rs3957357	AG		A	C-69T	+/-
GSTO1	rs11509438	GG		A	-2200G>A	-/-
GSTO1	rs4925	AA		A	C419A	+/+
GSTO2	rs156697	GG		A	A424G	-/-
GSTP1	rs1695	AA		G	GSTP1*B	-/-
GSTP1	rs1138272	CC		T	A114V	-/-
NOX	rs9932581	CC		T	-930G>A	-/-
SOD2	rs4880	AG		A	A16V	+/-
GPX1	rs1800668	AG		A	-46C>T	+/-
GPX4	rs713041	TT		T	C718T	+/+
CAT	rs769217	CC		T	1167C>T	-/-
CAT	rs1001179	TT		T	-262C>T	+/+
MPO	rs2243828	AA		G	2036A>G	-/-
GGT1	rs4820599	AA		G	-1207T>C	-/-

Biopterin

Gene	SNP rsID	Call	Impact	Variant Allele	Alias	Result
GCH1	rs841	NA		A	C243T	NA
NOS3	rs1800779	AA		G	A-922G	-/-
NOS3	rs3918226	CC		T	C-716T	-/-
NOS3	rs2070744	TT		C	T786C	-/-

• **A GCH1 Slow Haplotype Found**

-/- variant allele not present; +/- heterozygous genotype; +/+ homozygous genotype; +/+* hemizygous genotype (male X);
= much slower; = slower; = intermediate speed;
= faster; = much faster; = contextual; = unknown