

# Methylation Pathway Analysis

**JOHN DOE**

**DOB: 12 / 31 / 75**

**DATE OF  
ANALYSIS:**

11 · 15 · 23

All rights reserved. This work in whole or in part, may not be copied nor reproduced without the expressed written permission of Neurological Research Institute, LLC ("NRI"). © 2023, Neurological Research Institute, LLC

The information expressed in these documents does not constitute an attempt to practice medicine nor does it establish a doctor-patient relationship. This document is for informational and educational purposes only. Statements made in this document have not been evaluated by the U.S. Food & Drug Administration (FDA). The information provided is not intended to diagnose, treat, cure or prevent any disease or be used as the basis for treating a particular symptom or disease. Any products discussed or endorsed are not intended to diagnose, treat, cure or prevent any diseases or be used as the basis for treating a particular symptom or disease.

The information expressed in these documents is not meant to replace you working with a physician or health care practitioner when implementing any protocol discussed throughout these documents. Laboratory test results and comprehensive discussions or analysis of the laboratory results are intended to provide additional sources of information for you, and your physician or health care practitioner. Always seek the advice of your physician or other qualified health care practitioner with any questions you may have regarding your medical condition or as it specifically relates to implementing any protocols or suggestions discussed throughout this document. As always, consult with your health care professional.

# Table of Contents

INTRODUCTION	PAGE 1
COMMONLY ASKED QUESTIONS	PAGE 1
UNDERSTANDING THE BASICS	PAGE 2
HOW TO READ YOUR NUTRIGENOMIC RESULTS	PAGE 4
YOUR RESULTS	PAGE 7
THE YASKO METHYLATION PATHWAY	PAGE 8
NEXT STEPS: HOW TO MAKE THE MOST OUT OF YOUR GENETIC RESULTS	PAGE 9
<b>COMT</b>	<b>PAGE 11</b>
<b>VDR</b>	<b>PAGE 15</b>
<b>MAO A</b>	<b>PAGE 18</b>
<b>ACAT</b>	<b>PAGE 20</b>
<b>MTHFR</b>	<b>PAGE 22</b>
<b>MTR</b>	<b>PAGE 26</b>
<b>MTRR</b>	<b>PAGE 28</b>
<b>BHMT</b>	<b>PAGE 36</b>
<b>AHCY</b>	<b>PAGE 42</b>
<b>CBS</b>	<b>PAGE 46</b>
<b>SUOX</b>	<b>PAGE 50</b>
<b>SHMT</b>	<b>PAGE 52</b>
<b>NOS</b>	<b>PAGE 55</b>
ION TRANSPORT & ACE	PAGE 57
REFERENCES	PAGE 58

# Introduction

Dr. Amy Yasko designed the DNA Nutrigenomic Test to present data in a format that you can act on. The results of your test are integrated through a program called the Methylation Pathway Analysis (MPA). The Methylation Pathway Analysis uses Dr. Amy's knowledge base and expertise to provide recommendations tailored to your genetics.

This packet includes:

- Your results
- Information to help you understand how your genetics are a contributing factor to your health
- Guidance on how to begin supplementation personalized to your needs

Your genetics do not change over time, so suggestions that are made today can still be applied in the months and years to come!

Provided alongside your Methylation Pathway Analysis packet is our beginners guide to The Yasko Protocol, ***How to Get Started: Navigating Your Roadmap to Health***. We created this user-friendly guide for those who are interested in learning how to start The Yasko Protocol, which is centered around the results from your Methylation Pathway Analysis.

## Commonly Asked Questions

### WHAT IS THE METHYLATION PATHWAY ANALYSIS?

The Methylation Pathway Analysis is a guide that accompanies your DNA Nutrigenomic Test results. Your test results identify if there are genetic mutations in a nutritional pathway in your body, called the methylation cycle. The Methylation Pathway Analysis helps you take the next steps to understanding your results by providing information about each genetic mutation, and offers customized suggestions for supplementation and at-home test kits based on your genetics.

### WHAT MAKES OUR DNA NUTRIGENOMIC TEST UNIQUE?

Our DNA Nutrigenomic Test identifies a custom panel of 30 single nucleotide polymorphisms (SNPs), designed by Dr. Amy. The analysis includes supplement suggestions based on personalized results and provides a comprehensive assessment of the methylation cycle. Proper function of the methylation cycle is essential for several key pathways in the body. When genetic mutations, or “weaknesses”, are present in this cycle, there may be increased risk factors for a range of health concerns.



## WHAT DOES THE METHYLATION PATHWAY ANALYSIS DO FOR ME?

Dr. Amy likes to think of the Methylation Pathway Analysis as a road map. If you want to take a road trip from your hometown to a vacation destination of your choice (symbolic of your health goal!), you need a map with detailed directions. You'll want to know the best route to take to avoid damaged roads, closures, construction, and traffic.

Your Methylation Pathway Analysis tells you where all of these detours are located. With this knowledge, you can find the best way to get to where you want to go. The more information you have about genetic mutations in your pathway, the easier it is to create your road map and eliminate the guesswork on your journey to optimal health and wellness.

Because genetic mutations within the methylation cycle are well defined, the results from this test can help you decide what supports are best suited to address your SNPs. By understanding your nutritional needs and genetics, you can better manage your overall health and maintain proper function of the methylation cycle.

## HOW OFTEN DO I NEED TO RUN THIS TEST?

DNA testing gives you information about your genetics, so unlike biochemical tests where results may vary depending on your current health status, the **results of DNA testing will never change, meaning you only need to run this test once.**

### A NOTE FROM DR. AMY

Even one mutation in one of the 30 SNPs that this test measures provides critical information. Think about missing a critical piece of information along your route, which results in getting stuck for hours in traffic.

# Understanding the Basics

## WHAT IS THE METHYLATION CYCLE?

The methylation cycle is a key nutritional pathway in the body that is central to overall health and wellbeing. Genetic mutations present in this pathway have an impact on a wide range of health concerns, as well as a global impact on other genes in the body.

The body uses the methylation cycle to help edit and support multiple biochemical functions via the process of methylation. Having a balanced methylation cycle gives you the tools you need to help regulate numerous genes in your body.

## WHY IS THE METHYLATION CYCLE IMPORTANT?

Because the methylation cycle is central to the proper functioning of so many genes in the body, impairment (or genetic mutations) in this pathway can result in a variety of health conditions. However, because the methylation cycle is a nutritional pathway, you can support your body's genetic weaknesses with nutrients and supplementation.



## WHAT DO YOU MEAN BY GENETIC WEAKNESSES OR MUTATIONS?

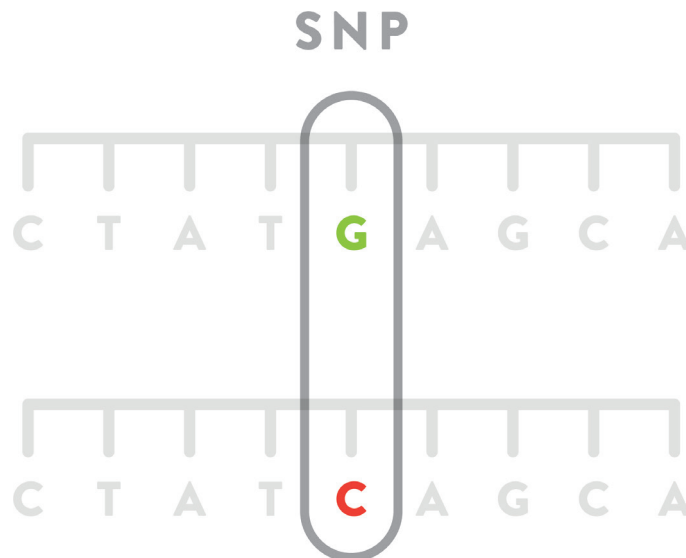
Single nucleotide polymorphisms (SNPs), pronounced “snips,” are variations in a DNA sequence. SNPs can also be referred to as genetic mutations. These variations occur when a single nucleotide (adenine, thymine, cytosine, or guanine) in a DNA sequence is altered.

An example of this is the substitution of a “C” (cytosine) for a “G” (guanine) in the sequence CTATGAGCA, resulting in the sequence CTATCAGCA.

There are approximately 25,000 genes in your body, some of which have SNPs (mutations) that can impact genetic function. Research has found a relationship between genetic variations (SNPs) and susceptibilities to certain health conditions.

### A NOTE FROM DR. AMY

The sequencing of the human genome opened up the possibility of comparing gene sequences of healthy individuals to those with mutations (changes in their genes), which lead to the identification of a number of health conditions associated with specific SNPs.



## WHAT HEALTH CONDITIONS ARE RELATED TO MUTATIONS (SNPS) IN THE METHYLATION CYCLE?

Common health conditions that have been associated with defects in methylation include diabetes, cardiovascular disease, thyroid dysfunction, neurological inflammation, chronic viral infection, neurotransmitter imbalances, atherosclerosis, cancer, aging, schizophrenia, decreased repair of tissue damage, improper immune function, neural tube defects, Down’s syndrome, multiple sclerosis, Huntington’s disease, Parkinson’s disease, Alzheimer’s disease, and autism spectrum disorder (ASD).<sup>1</sup>

It is important to note that the presence or absence of a reported SNP may be considered a contributing factor for a particular health condition, but should not be viewed as the sole determinant. *The results in this report should be interpreted in context, and with the guidance of your health care professional.*



## HOW MANY SNPS DOES THE DNA NUTRIGENOMIC TEST LOOK AT?

While there are thousands of genes and SNPs that can be examined, Dr. Amy has designed The DNA Nutrigenomic Test panel to focus on 30 SNPs that are part of the methylation cycle. This is a key nutritional pathway in the body that is central to health.

Many of the SNPs in Dr. Amy's custom panel are in the control or regulatory portion of the gene, meaning these SNPs can have a significant impact on your health. These include some of the more unique SNPs on this panel and are not always covered by other DNA profile tests.

## HOW DOES THIS INFORMATION SUPPORT MY HEALTH JOURNEY?

The DNA Nutrigenomic Test is a form of genetic testing that offers information you can act on. The results provide a molecular understanding of how foods and nutritional supplements can influence health and wellness driven by your unique genetic makeup.

**The beauty of looking at targeted SNPs in the methylation cycle is that it's a nutritional pathway, meaning if you find a mutation or imbalance in your system, you have ways to support or bypass them.**

The Methylation Pathway Analysis is custom designed to help you get the most out of your genetic results by offering information that can make a positive difference.

# How to Read Your Nutrigenomic Test Results

The DNA Nutrigenomic Test uses Dr. Amy's custom panel of 30 SNPs to identify if one or both copies of your genes have a mutation at a specific location in your DNA. Every person has two copies of each gene in their body, one copy comes from each parent.

Although mutations may occur throughout our lifetime, we are born with most of our SNPs. These SNP mutations are inherited and have been passed down from previous generations, and may offer explanations as to why certain diseases are prevalent in our families.

Having a gene with a SNP mutation does not mean that it is not functioning. It can mean that the gene is functioning at a higher than normal rate or at a decreased level.



## HOMOZYGOUS AND HETEROZYGOUS GENES

The terms homozygous and heterozygous are used to describe if both copies of your genes (remember you have two copies of each gene) are identical or different.



**Homozygous** means **both** copies of a gene are the **same**



**Heterozygous** means **one** copy of a gene is **different** than the other copy

The + and - designations refer to how the gene of interest compares to what is considered “normal.”



The ( - ) sign means there is no change present in this portion of your DNA sequence. There are no mutations present; you are homozygous for both copies of what is considered a “normal” gene.



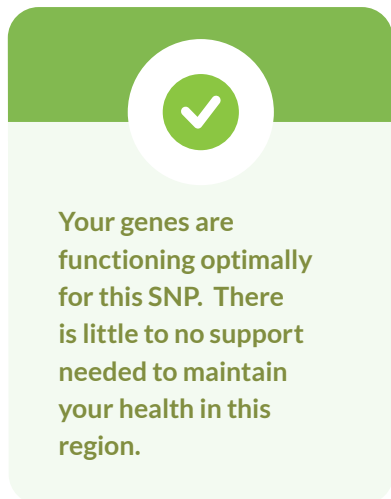
The ( + ) sign means your results show something different from “normal.” Both copies of your genes have the mutation, you have a homozygous mutation.



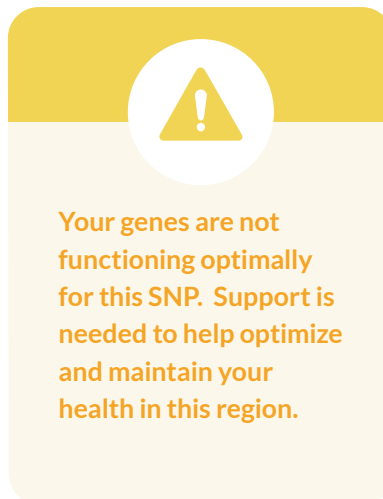
The ( + ) sign means your results show something different from “normal.” One out of the two copies of this gene have the mutation; you have a heterozygous mutation.

The reason this matters is because when BOTH copies of your DNA have a mutation (+/+), you may find that additional supplementation is needed to support health concerns associated with that mutation. For many, a homozygous (+/+) mutation may also be indicative of a highly sensitive system and a need to more gradually introduce new supplementation to address that particular SNP (mutation).

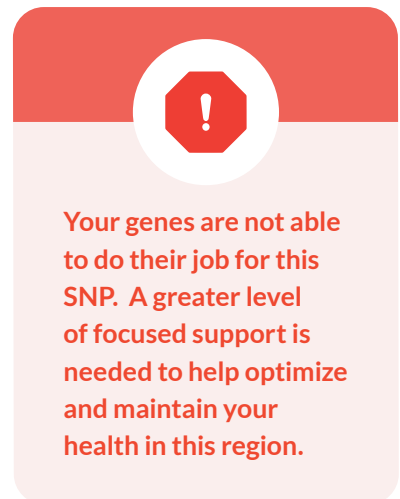
## GUIDE TO COLOR-CODED RESULTS



Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



Your genes are not functioning optimally for this SNP. Support is needed to help optimize and maintain your health in this region.



Your genes are not able to do their job for this SNP. A greater level of focused support is needed to help optimize and maintain your health in this region.



## WHAT IF I RAN MY GENETIC RESULTS WITH ANOTHER COMPANY?

The definition of what is “normal” can vary between labs and depends on what each lab uses as a reference database. Dr. Amy’s data-set is customized based on her knowledge of the genetic panel she created.

This means that the interpretation of results (+ and – symbols, and/or color-coded categories) may differ between labs. This is why you are also given the call letter for each SNP.

The call letter is your DNA base at a precise location on the gene and does not change between labs.

In cases where there is a discrepancy from one lab to another, for example one lab says your gene is (-/-), and the Methylation Pathway Analysis says the same gene is (+/+), you can refer to the call letter. The call letter represents the genetic results and does not change between labs, regardless of who you ran your test with.

### A NOTE FROM DR. AMY

An example Dr. Amy likes to use for the subjective interpretation of genetics is height:

If someone is 5’3” and stands next to someone who is 4’11”, they would be considered tall. If someone is 5’3” and stands next to someone who is 6’, they would be considered short. The person’s height is always 5’3”, but depending on what data set you compare them to, this person might be considered tall or short.





# Your Results

John Doe  
DOB: 8/15/1980

GENE	VARIATION	SNP	RESULT	CALL	
COMT	V158M	RS4680	- / -	G	
	H62H	RS4633	- / -	C	
	61	RS769224	- / -	G	
VDR	TAQ	RS731236	+ / -	HETERO	
	FOK	RS2228570	- / -	C	
MAO A	R297R	RS6323	- / -	G	
ACAT	1-02	RS3741049	+ / -	HETERO	
MTHFR	C677T	RS1801133	- / -	C	
	3	RS2066470	+ / -	HETERO	
	A1298C	RS1801131	+ / +	C	
MTR	A2756G	RS1805087	- / -	A	
MTRR	A66G	RS1801394	+ / +	G	
	H595Y	RS10380	- / -	C	
	K350A	RS162036	- / -	A	
	R415T	RS2287780	- / -	C	
	S257T	RS2303080	- / -	T	
	11	RS1802059	+ / -	HETERO	
	BHMT	1	RS585800	- / -	A
		2	RS567754	+ / -	HETERO
		4	RS617219	+ / -	HETERO
		8	RS651852	+ / +	T
AHCY	1	RS819147	- / -	A	
	2	RS819134	- / -	T	
	19	RS819171	- / -	A	
CBS	C699T	RS234706	+ / -	HETERO	
	A360A	RS1801181	+ / -	HETERO	
	N212N	RS2298758	- / -	C	
SUOX	S370S	RS773115	- / -	NO SUPPORT NEEDED	
SHMT	C1420T	RS1979277	+ / +	A	
NOS	D298E	RS1799983	- / -	G	





# The Yasko Methylation Pathway

The methylation pathway is a series of four connected cycles. Your body needs to navigate these four cycles in order to process nutrients properly.

Methylation is the transfer of a methyl group from one substance to another.<sup>a</sup> The substance that receives the donated methyl group becomes “methylated.” This process of moving methyl groups around is needed for several biochemical reactions in the body. If methylation is not functioning properly, a buildup of substrates and harmful end products can occur.

**As you read through your results, you can refer back to the Yasko Methylation Pathway to identify where each SNP is located in the pathway.**

## A NOTE FROM DR. AMY

I like to think of the methylation cycle as four traffic circles, and SNPs (mutations) as accidents or roadblocks within the circles. By identifying where to take alternative routes to bypass delays, you can move through the traffic circles more easily. Without this information, it is difficult to navigate around traffic, and a buildup of unfavorable compounds can occur.

## Next Steps: How To Make The Most Out Of Your Genetic Results

### A NOTE FROM DR. AMY

Research has shown that gene expression can be influenced by our environment, diet, toxic burden, and supplementation.

Understanding how to interpret your genetic results is an important first step in taking charge of your health. Your genetic results will never change, but you can alter how your genes are expressed when appropriate supports are put into place.

### WHAT DO I DO WITH MY RESULTS?

In this next section, we've organized your results by gene name and provided details about each SNP. With this information, you can identify the next steps you want to take based on your DNA results.

### HOW DO I KNOW WHAT SUPPLEMENTS WILL HELP SUPPORT MY SNPS?

There is a health category on [www.HolisticHeal.com](http://www.HolisticHeal.com) called “SNP Support.” If you have results that indicate you may benefit from supplementation for a specific SNP, you can refer directly to that SNP category to explore options best suited for that SNP. Links to each category are also listed within your results section for each SNP below.

**You do not need to use every supplement listed in each category!** Supplements are provided as options to discuss with your own health care professional, to gradually add in as you feel they are needed, and for additional consideration based on biochemical test results.

a. A methyl group is made up of one carbon atom and three hydrogen atoms (CH<sub>3</sub>).



## HOW CAN I BE SURE THE SUPPLEMENTS I'VE STARTED TAKING ARE HELPING?

Each SNP category includes biochemical tests that help to monitor progress for the supplements you have added. Biochemical testing measures the amount or activity of a particular enzyme or protein from a sample of urine, stool, saliva, or hair. All of the biochemical tests are at-home test kits and can be taken in the comfort of your own home.

### A NOTE FROM DR. AMY

While your DNA and SNPs do not change over time, your biochemical test results **do** change. Biochemical tests reflect progress in overcoming imbalances through the use of supplementation.

Dr. Amy is a strong believer in this type of testing, because it provides data that can be used to assess how well a supplement program is working for you. The results from follow-up biochemical testing verify if your supplementation plan is helping to achieve the goals you and your health care professional have set.

Each person is unique, so even if two individuals have identical DNA results, their biochemical test results will differ greatly depending on their lifestyle choices and experiences. For this reason, many individuals find it beneficial to look at both a DNA profile and data from biochemical tests to better customize a personalized supplement plan that works for them.

### A NOTE FROM DR. AMY

If you're interested in learning even more information about each SNP, explore my book ***Feel Good About Your SNPs.***

## CAN I BOOK A CONSULTATION WITH DR. AMY TO REVIEW MY RESULTS?

Dr. Amy no longer offers consultations as her waiting list became too extensive. In an effort to be able to help more people, Dr. Amy created The Yasko Protocol and offers several free resources so that individuals can follow her program while working with their own health care professional for additional support.

If you're looking for more guidance on what to do next, you can choose to receive a complimentary client file review on most of the biochemical tests offered on [www.HolisticHeal.com](http://www.HolisticHeal.com). The client file review includes Dr. Amy's personalized comments on your biochemical test results, in addition to her review of your genetic results and supplement list if you choose to provide them. As always, work with your health care professional to review suggestions and decide what will work best for you.

**If you're interested in learning more about The Yasko Protocol refer to our beginners guide, *How to Get Started: Navigating Your Roadmap to Health.***



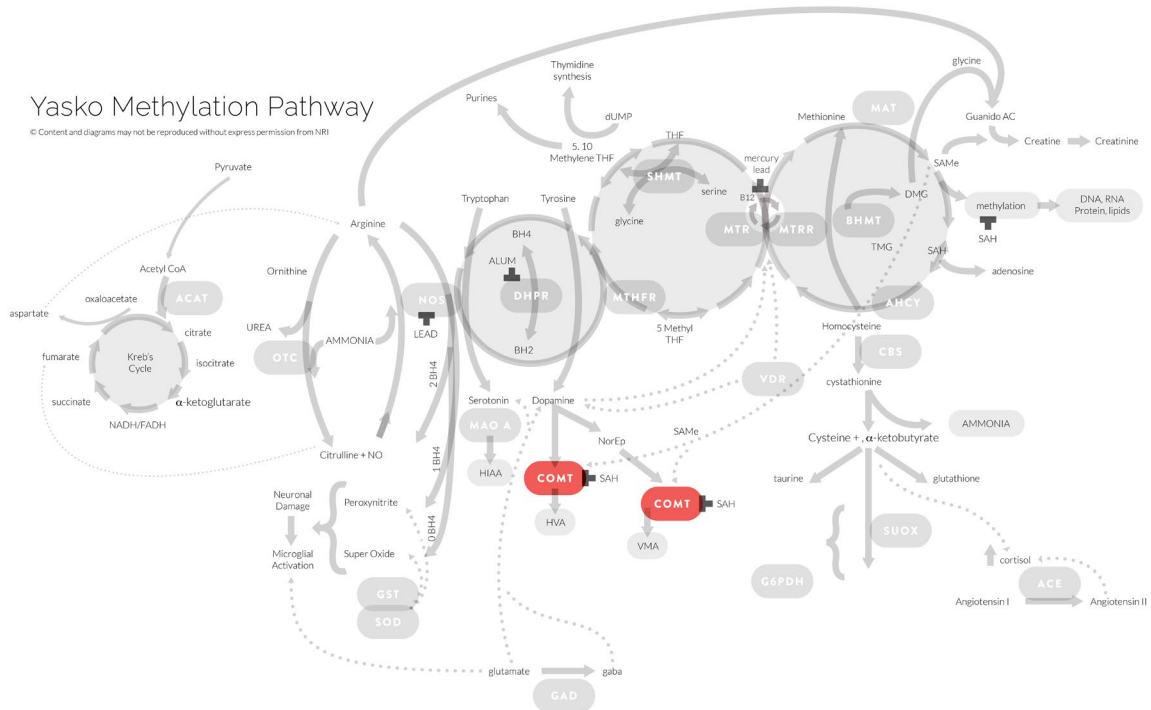
# COMT

The COMT gene gives your body instructions on how to make an enzyme called catechol-O-methyltransferase (COMT).<sup>2</sup>

In the brain, the COMT enzyme uses methyl groups to help breakdown different neurotransmitters, including dopamine, epinephrine, and norepinephrine. This process results in one of the major degradative pathways for this group of neurotransmitters, also referred to as catecholamines.<sup>3</sup>

Research has shown this group of neurotransmitters are involved in helping to regulate mood and attention (such as attention-deficit disorder [ADD]/attention-deficit hyperactivity disorder [ADHD], obsessive-compulsive disorder [OCD], and schizophrenia).<sup>4,5</sup> COMT has also been linked to the treatment of hypertension, asthma, Parkinson's disease, and proper use of estrogen in the body.<sup>3,6</sup> Increased sensitivity to pain has recently been associated with COMT activity.<sup>7</sup>

**To find out more about COMT explore Dr. Amy's book, *Feel Good About Your SNPs*.**



COMT V158M



TEST RESULT **-/- (NO MUTATION)**  
 VARIATION **NONE (V158M NOT PRESENT)**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

Both genes for COMT located at RS4680 are functioning optimally for your health!  
 May have a greater need for methyl donors (ex: S-AMe, methyl-B12). Individuals who are COMT -/- tend to have balanced levels of dopamine due to consistent COMT activity.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports methyl donors and basic methylation support.

- All In One multivitamin
- COMT V158M -/- nucleotide blend
- Curcumin or Turmeric
- DHA
- Methyl-B12
- Quercetin
- S-AMe

**CLICK HERE**

TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess levels of lithium, arsenic, and cobalt.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.



COMT H62H



**TEST RESULT**    **-/- (NO MUTATION)**  
**VARIATION**    **NONE (H62H NOT PRESENT)**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

Both genes for COMT located at RS4633 are functioning optimally for your health!  
 May have a greater need for methyl donors (ex: SAmE, methyl-B12). Individuals who are COMT H62H -/- tend to have balanced levels of dopamine due to consistent COMT activity.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports methyl donors and basic methylation support.

- All In One multivitamin
- Curcumin or Turmeric
- DHA
- Methyl-B12
- Quercetin
- SAmE

**CLICK HERE**

TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess levels of lithium, arsenic, and cobalt.  
 Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.





**TEST RESULT** +/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)  
**VARIATION** 61



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May have difficulty tolerating methyl donors (ex: SAMe, methyl-B12). May be more susceptible to fluctuations in dopamine levels and issues with attention/focus.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports mood, attention, and basic methylation support. Support your inflammatory pathway if you have a lower tolerance for pain and avoid supplementation that contains methyl donors.

- All In One multivitamin
- Boswellia
- COMT +/- nucleotide blend
- Curcumin or Turmeric
- DHA
- Essential mineral supplementation
- GABA
- Lemon balm (Melissa)
- Liquid methyl-folate
- Lithium
- Nettle
- Phosphatidylserine
- Valerian root

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess levels of lithium, arsenic, and cobalt.

If attention issues are present, consider an at-home test kit that measures neurotransmitter levels to assess epinephrine and norepinephrine levels.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.







VDR TAQ



TEST RESULT  
VARIATION

**+/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)**  
**TAQ**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Individuals who are VDR +/- may be more sensitive to supplementation with methyl donors (ex: SAME, methyl-B12).

Individuals with a VDR +/- status and a COMT ++ mutation may have cumulative effects and have a greater susceptibility to fluctuations in dopamine levels and issues with attention/focus.

**OPTIMIZE WHAT  
YOU'VE GOT**

Consider supplementation that supports mood, attention, and basic methylation support.

- All In One multivitamin
- DHA
- GABA
- Lithium
- Phosphatidylserine

[CLICK HERE](#)

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR  
PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess levels of lithium, arsenic, and cobalt.

If attention issues are present, consider an at-home test kit that measures neurotransmitter levels to assess epinephrine and norepinephrine levels.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.



VDR FOK



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (FOK NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for VDR located at RS2228570 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



# MAO A

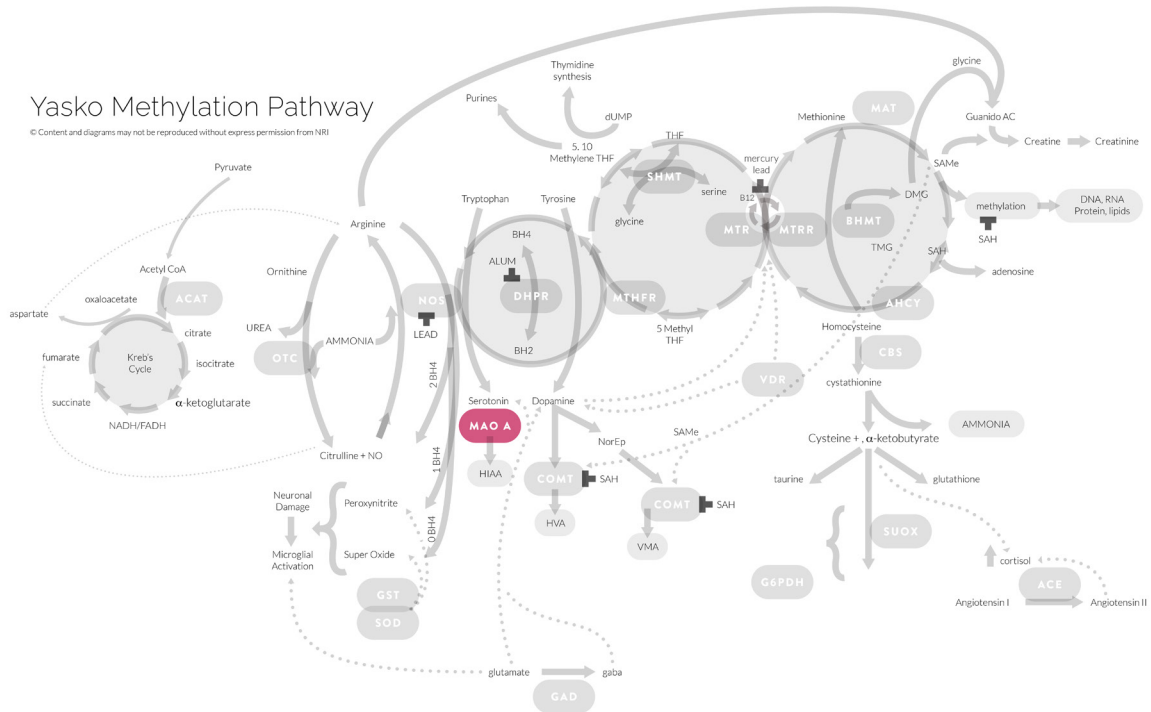
The MAO A gene gives your body instructions on how to make an enzyme called monoamine oxidase A (Mao A). This enzyme helps breakdown certain neurotransmitters, including serotonin, norepinephrine, and dopamine.<sup>14</sup>

Changes in how this enzyme functions can result in neurotransmitter imbalances, which can impact behavior and emotion. For example, imbalances in the neurotransmitter serotonin have been associated with mood, depression, aggression, anxiety, and obsessive-compulsive behavior.<sup>15,16</sup>

Because of the impact this gene has on neurotransmitter function, MAO A has been associated with various psychiatric disorders, including antisocial behavior.<sup>14</sup>

MAO A is inherited with the X chromosome. Females have two X chromosomes (one from each parent), and males have one X chromosome (from their mother). This means that a MAO A mutation from the father will not be inherited by sons. Conversely, female genetics will reflect the MAO A status from both parents.<sup>16</sup>

**To find out more about MAO A explore Dr. Amy's book, *Feel Good About Your SNPs*.**



MAO A R297R



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (R297R NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for MAO A located at RS6323 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

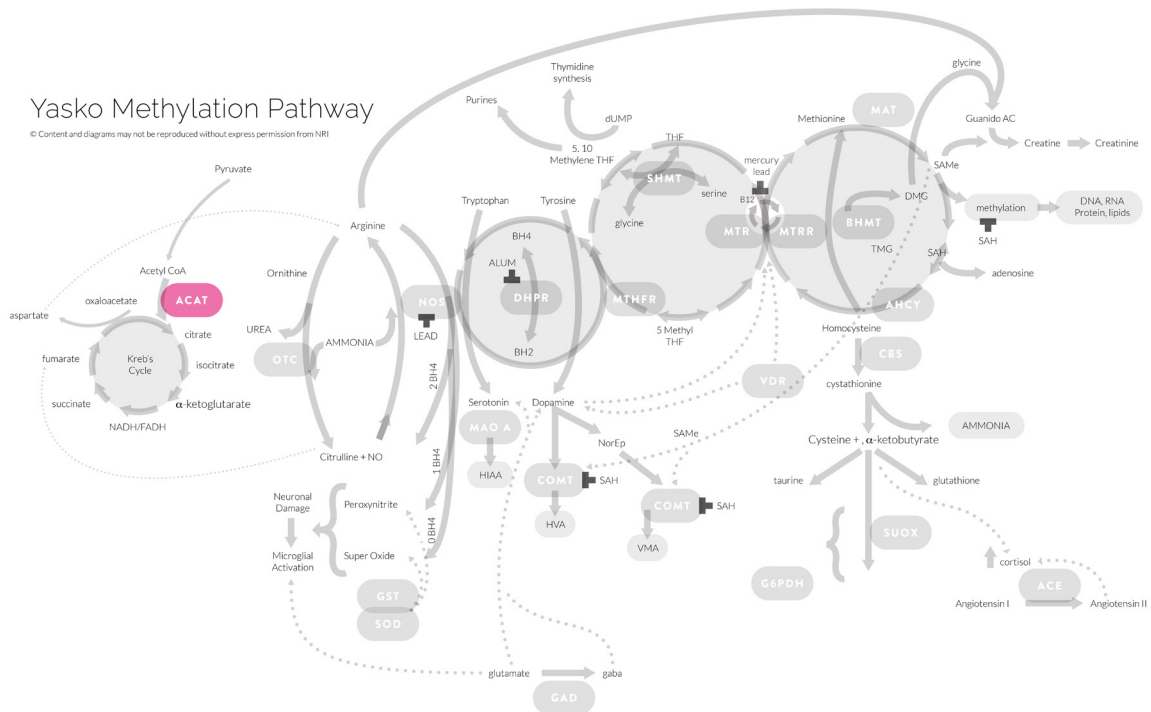


# ACAT

The ACAT gene gives your body instructions on how to make the enzyme acetyl coenzyme A acetyltransferase (ACAT). This enzyme is found in the mitochondria in cells and converts one molecule (acetoacetyl-CoA) into two smaller molecules (acetyl-CoA) that are involved in producing energy. Because of this, ACAT is a factor in generating energy for cells.<sup>17</sup>

ACAT helps process ketones (which are produced when the body breaks down fats) and isoleucine (a building block for several proteins), and plays a role in cholesterol balance in the body by helping to prevent excess cholesterol from accumulating in certain parts of cells in the body.<sup>18</sup> Increases in the presence of ACAT may contribute to higher levels of cholesterol and possible imbalances in fatty acid digestion.<sup>19</sup>

**To find out more about ACAT explore Dr. Amy's book, *Feel Good About Your SNPs*.**



ACAT 1-02



TEST RESULT **+/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)**  
VARIATION **1-02**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May be more susceptible to difficulty digesting fats, cholesterol, and the ability to process the conversion of fats into energy.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports fat digestion, conversion of food into energy, helps combat issues caused by harmful bacteria, and offers basic methylation support.

- ACAT+ nucleotide blend
- All In One multivitamin
- B-Complex
- Biotin
- Chitosan (if no shellfish allergy)
- CoQ10
- Digestive enzymes (including pancreatin)
- DHA
- EDTA
- L-carnitine
- Lactase
- Mitochondrial support
- NADH
- Support fat digestion and bile fats

[CLICK HERE](#)

TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.

**TRACK YOUR PROGRESS**

Use an at-home test kit that monitors levels of lactate and pyruvate to assess the ability to convert food into energy and to check for ketones.

Use an at-home test kit that measures toxic elements and nutritional elements to assess lithium levels.

If experiencing gut issues, consider an at-home gastrointestinal test to check for the presence of gut bugs and presence of mycoplasma.

If concerned about thyroid or weight issues, utilize an at-home thyroid test kit.

Work with your health care professional to monitor cholesterol levels.



# MTHFR

The MTHFR gene gives your body instructions on how to make the enzyme methylenetetrahydrofolate reductase (MTHFR). This enzyme is involved in processing amino acids, which are the building blocks of proteins.<sup>20</sup>

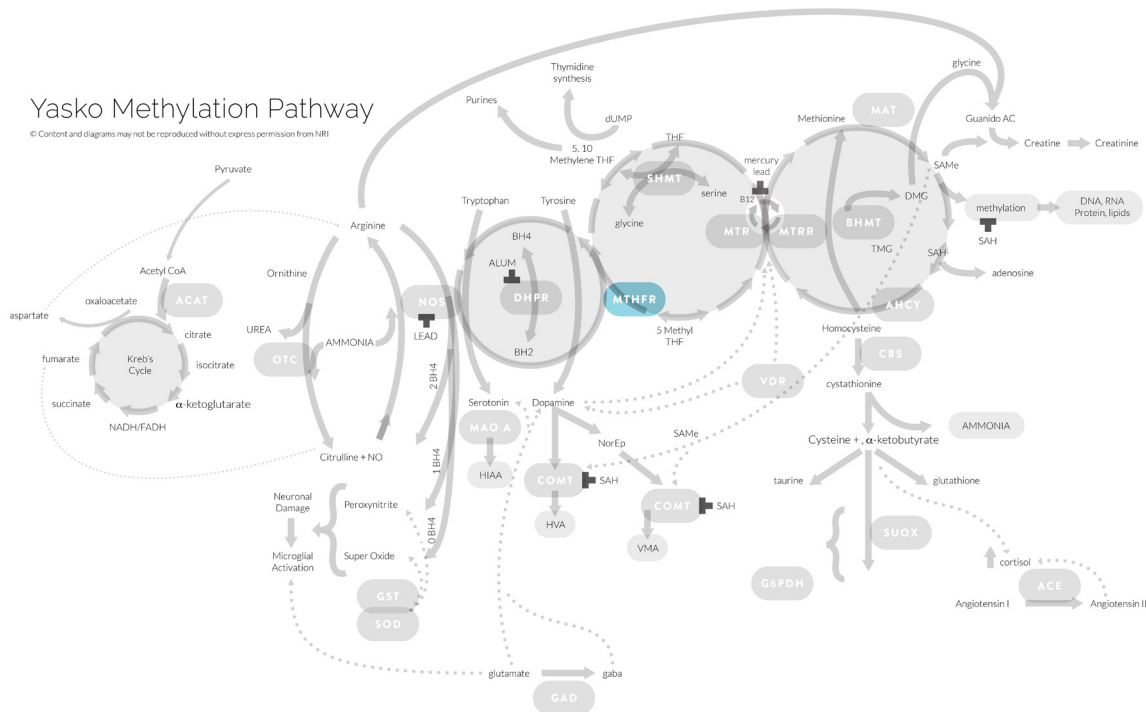
The MTHFR gene product is located at a critical point in the methylation cycle. MTHFR helps your body maintain normal levels of homocysteine and methionine by facilitating an important reaction that converts a form of folate (vitamin B9) called 5,10-methylenetetrahydrofolate to a different form of folate called 5-methyltetrahydrofolate, which is the main form of folate found in blood.<sup>21</sup> This reaction is needed for your body to be able to convert homocysteine (an amino acid) into methionine, which is a fundamental amino acid that your body needs.<sup>20</sup>

There are three SNPs in the MTHFR gene that Dr. Amy looks at: MTHFR C677T, MTHFR 3, and MTHFR A1298C.

Several mutations in the MTHFR gene have been well characterized and have been associated with homocystinuria (inability for your body to process methionine), developmental delays, psychiatric disorders, later-onset neurodegenerative disorders, stroke, heart disease, cancer, and may play a role in miscarriages, as well as other health conditions.<sup>22-24</sup>

SNPs in MTHFR may display cumulative effects if you also have SNPs in MTR, MTRR, AHCY, or CBS.

**To find out more about MTHFR explore Dr. Amy's book, *Feel Good About Your SNPs*.**





MTHFR C677T



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (C677T NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for MTHFR located at RS1801131 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



MTHFR 3



TEST RESULT **+/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)**  
 VARIATION **3**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May be more susceptible to severe issues with methylation and the ability to process homocysteine, which results in elevated homocysteine levels.

Elevated levels of homocysteine can cause excess formation of S-adenosyl homocysteine (SAH) which can prevent important reactions that are involved in methylation of DNA, RNA, neurotransmitters, and phospholipids.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports the breakdown of methionine, provides adequate support of methyl-B12 and folate, and offers basic methylation support.

- All In One multivitamin
- DHA
- Liquid methyl-folate
- MTHFR 3+ nucleotide blend
- Phosphatidylserine

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess lithium levels.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.



MTHFR A1298C



TEST RESULT  
VARIATION

**+/+ (MUTATIONS IN BOTH OF YOUR TWO GENES)**  
**A1298C**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Homozygous mutation

*Be sure to work closely with your health care professional for this type of mutation, it's likely you will benefit from extra support on your health journey.*

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

May be more susceptible to fluctuations in serotonin and dopamine levels, which can present as mood disorders.

Dr. Amy's research supports the idea that the A1289C mutation is associated with an inability to convert BH2 to BH4, which may result in exceedingly low BH4 levels.

Low levels of BH4 are associated with severe parasitic infections, diabetes, hypertension, and arteriosclerosis. BH4 is needed to produce serotonin and dopamine, and for detoxification of ammonia.

Individuals that also have CBS C699T mutations may have elevated levels of ammonia that need to be detoxified.

**OPTIMIZE WHAT  
YOU'VE GOT**

Keeping ammonia levels under control is of paramount importance for overall health and wellness. Excess ammonia can drain already limited levels of BH4 in individuals with this mutation.

Avoiding lifestyle choices that can increase ammonia levels, such as high protein diets, may be beneficial. Consider supplementation that supports gentle detox of ammonia and supports mood and basic methylation support.

- All In One multivitamin
- Beef liver
- BH4 support
- DHA
- EDTA
- Horsetail grass
- MTHFR A1298C+ nucleotide blend
- Selenium

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR  
PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess levels of aluminum and other metals that can impair BH4 levels.

Monitor levels of amino acids and neurotransmitters to assess if tryptophan and tyrosine are being converted to serotonin and dopamine.

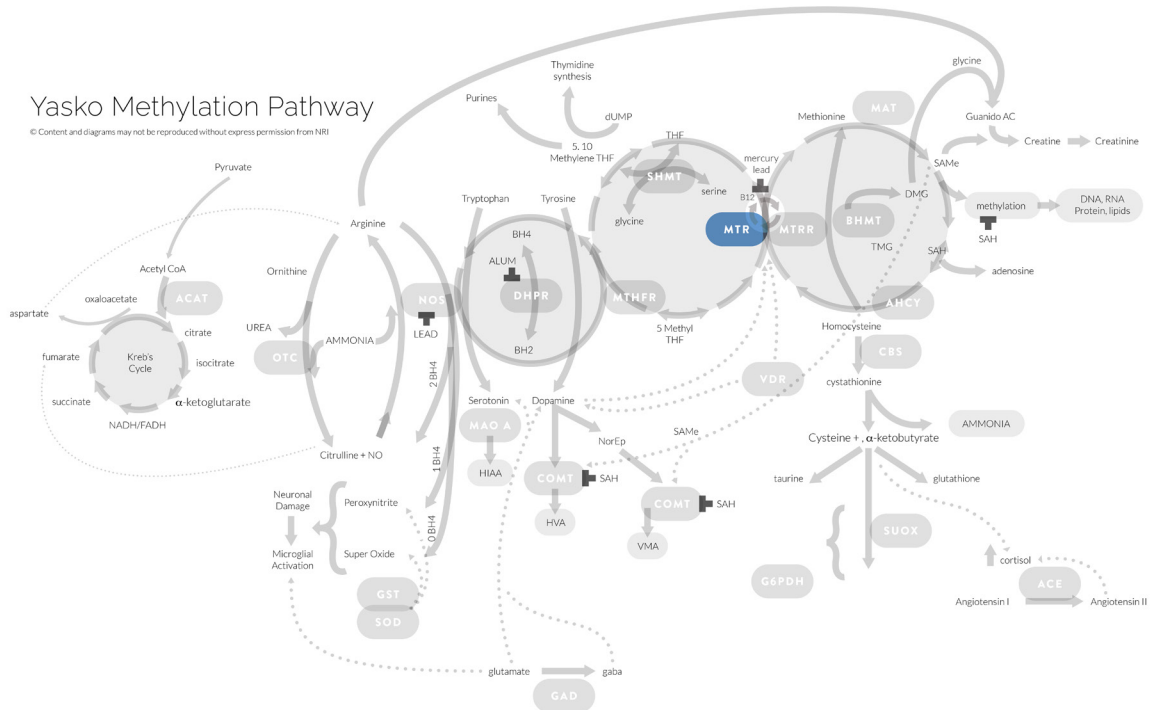


# MTR

The MTR gene gives your body instructions on how to make the enzyme methionine synthase. This enzyme works together with another gene product (MTRR) to regenerate and utilize methyl cobalamin (a form of vitamin B12) in the methylation cycle to help convert homocysteine to methionine.<sup>25</sup> Methionine is a fundamental amino acid that your body needs.

Mutations in MTR have been associated with methyl cobalamin deficiency and high levels of homocysteine.<sup>26</sup> High homocysteine levels may be a risk factor for heart disease and Alzheimer's disease.<sup>27,28</sup>

**To find out more about MTR explore Dr. Amy's book, *Feel Good About Your SNPs*.**



MTR A2756G



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (A2756G NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for MTR located at RS1805087 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



## MTRR

The MTRR gene gives your body instructions on how to make the enzyme methionine synthase reductase. This enzyme is important for folate metabolism and cellular methylation.<sup>29</sup>

MTRR works together with methionine synthase (MTR) to recycle homocysteine back into methionine.<sup>30</sup> It does this by regenerating methylcobalamin B12 so that MTR is able to utilize it.

Mutations that impair the function of MTRR have secondary consequences on the activity of the MTR gene. Even if you have no mutations in MTR, if MTRR is not able to function properly, MTR will not have enough methylcobalamin B12 to work optimally in the methylation cycle.

The combination of a mutation in MTRR, which compromises its ability to regenerate methylcobalamin B12, and an MTR mutation that allows your body to use B12 at an accelerated rate, can result in extremely depleted levels of methylcobalamin B12 in the body.

MTRR and MTR are part of what is commonly referred to as the “long route” of the methylation cycle. When MTRR or MTR do not function properly, or when there is not enough methylcobalamin B12 for the body to use, methionine is not effectively produced via the “long route.” The result of this is more pressure on the “short route” of the methylation cycle, which involves the BHMT gene.

MTRR polymorphisms may have cumulative effects with MTHFR/C677T, MTR, AHCY, or CBS polymorphisms.

There are six SNPs in MTRR that Dr. Amy looks at: A66G, H595Y, K350A, R415T, S257T, and 11.

Dr. Amy has observed that the MTRR 11 SNP has a different impact on the methylation cycle than the MTRR SNPs described above. Those who are MTRR 11 (+/-), and particularly those who are MTRR 11 (+/+), tend to have issues with intestinal permeability and leaky gut. These differences are noted in the SNP tables for individuals who have this mutation.

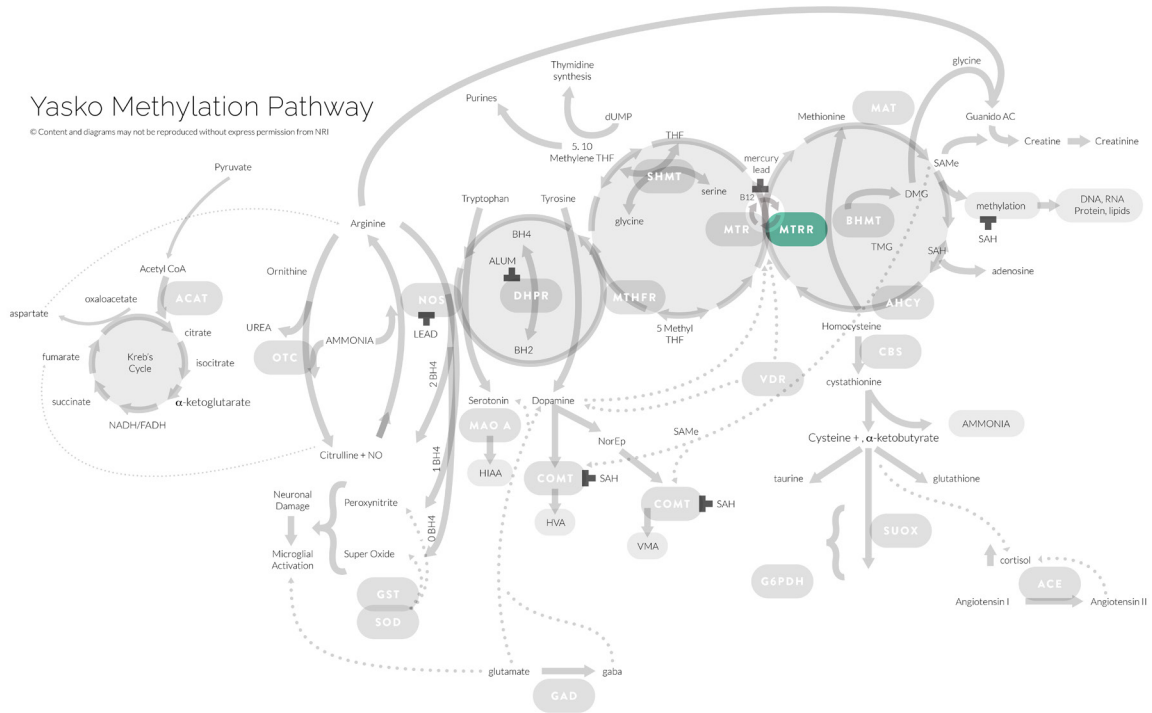
**To find out more about MTRR explore Dr. Amy’s book, *Feel Good About Your SNPs*.**

### A NOTE FROM DR. AMY

Extremely low levels of B12 create a roadblock in the methylation pathway between methionine and homocysteine. This roadblock requires a nutritional bypass to restore pathway function.



# MTRR



MTRR A66G



TEST RESULT **+/+ (MUTATIONS IN BOTH OF YOUR TWO GENES)**  
 VARIATION **A66G**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Homozygous mutation

*Be sure to work closely with your health care professional for this type of mutation, it's likely you will benefit from extra support on your health journey.*

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May be more susceptible to high levels of homocysteine, which can impact activity of the methylation pathway.

Individuals with this mutation and a MTR +/+ mutation may have cumulative effects.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports B12, folate, and basic methylation support. Individuals with this SNP may find hydroxocobalamin B12 more suitable.

Focusing on nutritional care for the "short route" of the methylation pathway while working to improve activity of the "long route" of the methylation pathway may be beneficial.

- Additional B12 (if lithium levels are in balance)
- All In One multivitamin
- DHA
- Intrinsic factor (support B12 transport)
- MTR/MTRR+ nucleotide blend
- Phosphatidylserine

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to regularly assess lithium and iodine levels. Closely monitor lithium to ensure it is in balance before further supplementation of your methylation pathway.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.

Assess toxic and essential elements to evaluate cobalt levels.





MTRR H595Y



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (H595Y NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for MTRR located at RS10380 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



MTRR K350A



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (K350A NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for MTRR located at RS162036 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



MTRR R415T



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (R415T NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for MTRR located at RS2287780 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



MTRR S257T



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (S257T NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for MTRR located at RS2303080 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



MTRR 11



TEST RESULT **+/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)**  
 VARIATION **11**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May be more susceptible to experiencing issues with intestinal permeability and leaky gut.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports balanced protein levels and a healthy gut lining, provides energy for nutrient transport, offers inflammatory pathway support, and basic methylation support.

- All In One multivitamin
- Amino acids
- ATP
- Basic mineral support
- Boswellia
- Colostrum (general support for gut lining)
- Curcumin or Turmeric
- DHA
- Mitochondrial support
- MTRR 11+ nucleotide blend
- Nettle

[CLICK HERE](#)

TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON [HOLISTICHEAL.COM](https://www.holisticheal.com) TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess the extent of mineral excretion.

Use an at-home test kit that measures levels of amino acids to assess for overall amino acid excretion.

Consider using a gastrointestinal test to evaluate microbial imbalances, and check for intestinal permeability.



## BHMT

The BHMT gene gives your body instructions on how to make the enzyme betaine homocysteine methyltransferase. This enzyme is found primarily in the liver and kidney. It facilitates the conversion of betaine to dimethylglycine, and homocysteine to methionine.<sup>31</sup> This reaction is commonly referred to as the “short route” of the methylation cycle.

BHMT offers a secondary route in the methylation cycle for the conversion of homocysteine to methionine that does not require methylcobalamin B12. The BHMT enzyme utilizes either trimethylglycine (TMG) betaine or phosphatidylserine as starting material to convert homocysteine to methionine.<sup>32,33</sup>

Because BHMT plays a role in the regulation and metabolism of homocysteine, mutations in this gene will likely present as elevated homocysteine levels. The BHMT dependent conversion of homocysteine to methionine can be affected by stress, cortisol, and may play a role in ADD/ADHD due to the impact it has on norepinephrine levels.<sup>34,35</sup>

### A NOTE FROM DR. AMY

MTHFR, MTR, and MTRR are involved in the “long route” around the methylation cycle, which depends on B12.

### A NOTE FROM DR. AMY

Because BHMT is central to the “short route”, I use it as a great starting point to help balance the methylation cycle.

There are four SNPs in BHMT that Dr. Amy looks at: 1, 2, 4, and 8. Dr. Amy has observed that BHMT 8 appears to have a more pronounced effect than BHMT 1, 2, and 4 on BHMT activity. Those who have mutations in BHMT 8 may find they need extra support to compensate for the SNP. Homozygote (+/+) mutations tend to be more influenced than heterozygote (+/-) mutations.

**To find out more about BHMT explore Dr. Amy’s book, *Feel Good About Your SNPs*.**





BHMT 1



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (1 IS NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for BHMT located at RS585800 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.







**TEST RESULT** +/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)  
**VARIATION** 2



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May require extensive and focused support to achieve proper methylation.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports both the “short route” of the methylation cycle as well as the methionine synthase dependent “long route” of the methylation pathway.

- All In One multivitamin
- Adrenal support
- DHA
- Phosphatidylserine

**CLICK HERE**

**TO VISIT THE “SNP SUPPORT” HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY’S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess lithium levels, excess thorium, vanadium, and molybdenum (which may indicate the presence of high taurine and issues processing sulfur).

If attention issues are present, consider an at-home test kit that measures neurotransmitter levels to assess epinephrine and norepinephrine.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they’re not too high in comparison to s-adenosyl, taurine, and methionine levels.





TEST RESULT **+/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)**  
VARIATION **4**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May require extensive and focused support to achieve proper methylation.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports both the “short route” of the methylation cycle as well as the methionine synthase dependent “long route” of the methylation pathway.

- All In One multivitamin
- Adrenal support
- DHA
- Phosphatidylserine

**CLICK HERE**

**TO VISIT THE “SNP SUPPORT” HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY’S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess lithium levels, excess thorium, vanadium, and molybdenum (which may indicate the presence of high taurine and issues processing sulfur).

If attention issues are present, consider an at-home test kit that measures neurotransmitter levels to assess epinephrine and norepinephrine.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they’re not too high in comparison to s-adenosyl, taurine, and methionine levels.





TEST RESULT **+/+ (MUTATIONS IN BOTH OF YOUR TWO GENES)**  
 VARIATION **1**



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Homozygous mutation

*Be sure to work closely with your health care professional for this type of mutation, it's likely you will benefit from extra support on your health journey.*

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May have trouble regulating blood sugar and insulin levels. Difficulty regulating blood sugar can cause inflammation.

Those who have mutations in BHMT 8 may find they need focused pancreatic support.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that supports the pancreas and healthy blood sugar levels.

- All In One multivitamin
- Banaba leaf
- Chromium
- Digestive enzymes (including pancreatin)
- DHA
- Gymnema sylvestre
- Lithium (low dose)
- Phosphatidylserine
- Potassium (low dose)
- Vanadium

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess lithium levels, excess thorium, vanadium, and molybdenum (which may indicate the presence of high taurine and issues processing sulfur).

If attention issues are present, consider an at-home test kit that measures neurotransmitter levels to assess epinephrine and norepinephrine.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.

Work with your health care professional to check blood sugar, HbA1c and insulin levels regularly.



# AHCY

The AHCY gene gives your body instructions on how to make the enzyme S-adenosylhomocysteine hydrolase. This enzyme is involved in a multistep process that breaks down methionine into adenosine and homocysteine via S-adenosylhomocysteine (SAH).<sup>36,37</sup>

SAH is a very potent inhibitor of S-adenosyl-L-methionine (SAME), which is the most important methyl donor in the body. AHCY sits downstream from SAME; the activity of AHCY can therefore indirectly impact SAME levels (via SAH) and as a result impact methylation.<sup>38</sup>

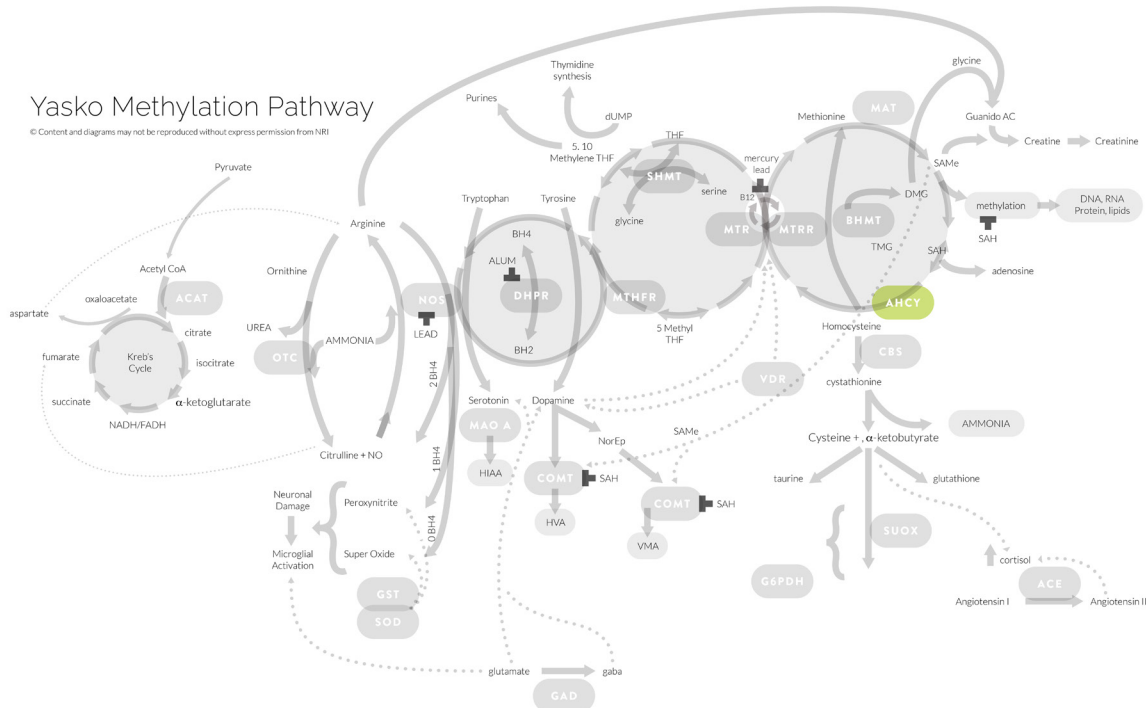
There are three SNPs in AHCY that Dr. Amy looks at: 1, 2, and 19. AHCY 1 mutations may contribute to increased methionine levels, and AHCY 1 and 2 mutations may increase SAH levels.

Increased levels of homocysteine and SAH have been associated with cardiovascular disease, vascular thrombosis, neural tube defects, cerebrovascular disease, dementia-like symptoms, and oxidative stress.<sup>28</sup>

## A NOTE FROM DR. AMY

Methylation is a critical reaction in the body and is important for the regulation of DNA, RNA, neurotransmitters, and phospholipids. I consider AHCY SNPs an overriding priority when making choices for supplementation because of the significant impact it has on SAME and methylation in the body.

**To find out more about AHCY explore Dr. Amy's book, *Feel Good About Your SNPs*.**



AHCY 1



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (1 NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for AHCY located at RS819147 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



AHCY 2



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (2 NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for AHCY located at RS819134 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



AHCY 19



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (19 NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for AHCY located at RS819171 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



# CBS

The CBS gene gives your body instructions on how to make the enzyme cystathionine beta-synthase.<sup>39</sup> This enzyme uses vitamin B6 to convert homocysteine and serine into cystathionine (the precursor of cysteine). This reaction allows methionine and homocysteine to be excreted from the methylation pathway.<sup>39</sup>

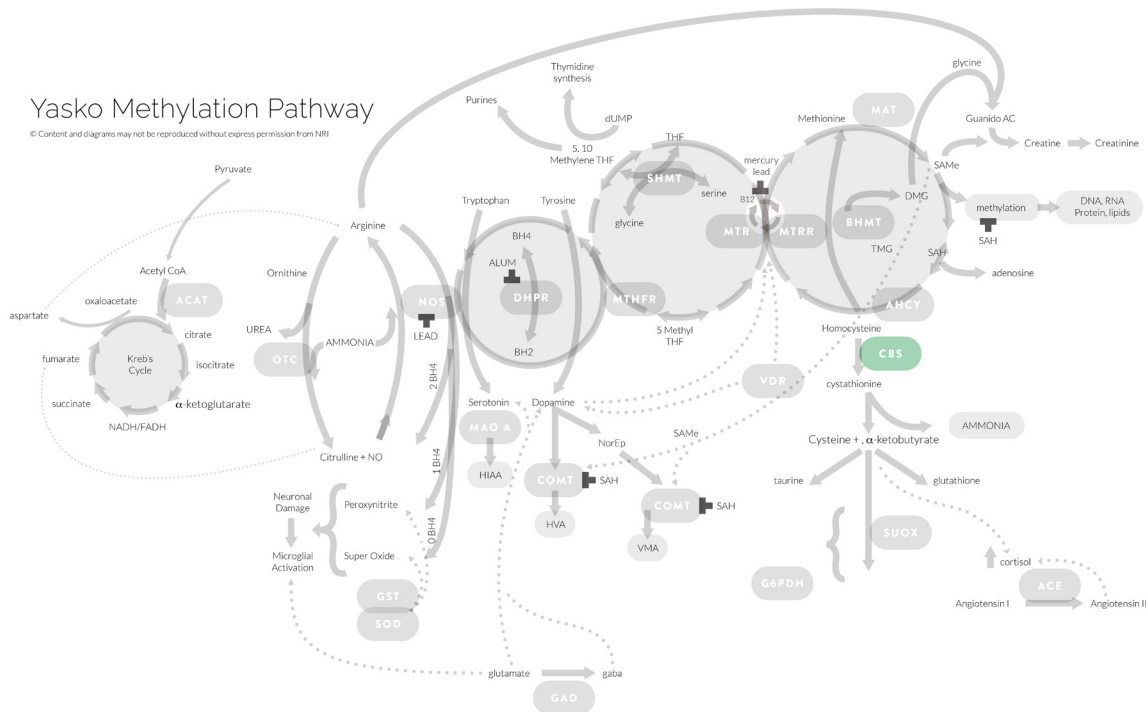
The CBS enzyme acts as a gate between homocysteine and the downstream portion of the methylation pathway, which is responsible for generating ammonia in the body. Deficiencies in this gene can cause cystathionine beta-synthase deficiency (CBSD), which can lead to homocystinuria.<sup>40</sup>

The CBS mutations that are identified in this SNP panel focus on increased CBS activity, and consequently increased activity of the CBS enzyme.<sup>41-46</sup> Increased activity of both the gene and enzyme can result in the depletion of other segments of the methylation pathway, including supplemented B12 that is administered to address other mutations.

CBS function is influenced by vitamin B6, individual betaine and folate levels, and may have cumulative effects with MTHFR SNPs. Harmful gut microbes, oxidative stress, and SAME supplementation can also contribute to increased CBS activity.<sup>47,48</sup>

There are three SNPs in CBS that Dr. Amy looks at: A360A, C699T, and N212N.

**To find out more about CBS explore Dr. Amy's book, *Feel Good About Your SNPs*.**





CBS C699T



**TEST RESULT** +/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)  
**VARIATION** C699T



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May be more susceptible to sensitivity to sulfur products and sulfur containing antibiotics.  
 May display excessively high taurine levels in urine amino acid tests following supplementation for methylation support.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that offers adrenal support, antioxidant support, and basic methylation support.

- Adrenal support
- All In One multivitamin
- Antioxidant support
- CBS+ nucleotide blend (recommended to check taurine levels after 4-6 weeks of use)
- DHA
- Hydroxy-B12, Adenosyl-B12, and Methyl-B12 (as tolerated)
- Molybdenum
- Phosphatidylserine

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess lithium, molybdenum, boron, and vanadium levels.

Use an at-home test kit that measures amino acids to regularly check taurine levels.

If experiencing gut issues, consider an at-home gastrointestinal test to check for the presence of gut bugs.

If attention issues are present, consider an at-home test kit that measures neurotransmitter levels to assess epinephrine and norepinephrine.



CBS A360A



**TEST RESULT** +/- (SINGLE MUTATION IN ONE OF YOUR TWO GENES)  
**VARIATION** A360A



**THE YASKO PROTOCOL CONSIDERS THIS RESULT**

Heterozygous mutation

**POSSIBLE ASSOCIATED HEALTH CONCERNS**

May be more susceptible to sensitivity to sulfur products and sulfur containing antibiotics.  
 May display excessively high taurine levels in urine amino acid tests following supplementation for methylation support.

**OPTIMIZE WHAT YOU'VE GOT**

Consider supplementation that offers adrenal support, antioxidant support, and basic methylation support.

- Adrenal support
- All In One multivitamin
- Antioxidant support
- CBS+ nucleotide blend (recommended to check taurine levels after 4-6 weeks of use)
- DHA
- Hydroxy-B12, Adenosyl-B12, and Methyl-B12 (as tolerated)
- Molybdenum
- Phosphatidylserine

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess lithium, molybdenum, boron, and vanadium levels.

Use an at-home test kit that measures amino acids to regularly check taurine levels.

If experiencing gut issues, consider an at-home gastrointestinal test to check for the presence of gut bugs.

If attention issues are present, consider an at-home test kit that measures neurotransmitter levels to assess epinephrine and norepinephrine.



CBS N212N



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (N212N NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for AHCY located at RS2298758 are functioning optimally for your health, you're all set!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



# SUOX

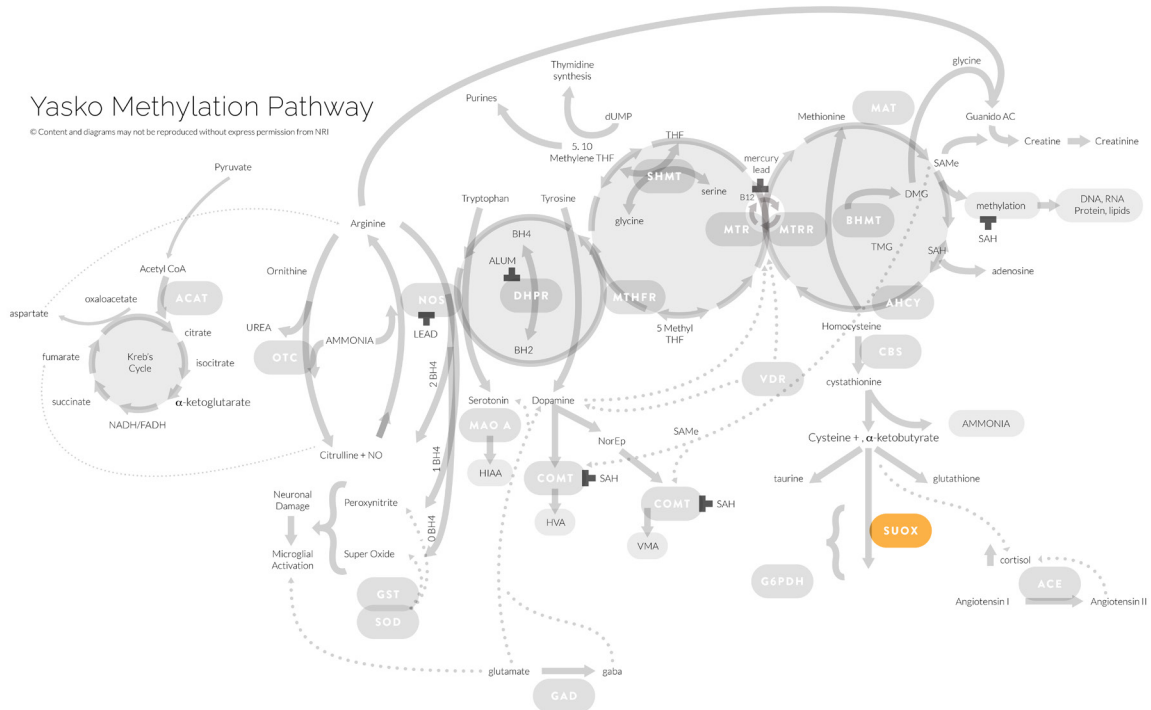
The SUOX gene gives your body instructions on how to make the enzyme sulfite oxidase. This enzyme helps break down amino acids containing sulfur that your body no longer needs. It does this by facilitating the conversion of sulfite to sulfate.<sup>49,50</sup>

The critical role of the SUOX enzyme is to detoxify sulfites in the body. Sulfites are generated as a natural byproduct of the methylation cycle and can also be ingested from the food that we eat. Exposure to sulfites can induce a range of adverse effects in sensitive individuals, including dermatitis, hives, flushing, abdominal pain and diarrhea, and anaphylactic and asthmatic reactions.<sup>51</sup>

Mutations in SUOX may be a risk factor for isolated sulfite oxidase deficiency and polycystic ovarian syndrome.<sup>50,52</sup>

The SUOX SNP that Dr. Amy focuses on is a mutation that results in decreased SUOX activity.

**To find out more about SUOX explore Dr. Amy's book, *Feel Good About Your SNPs*.**



SUOX S370S



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (S370S NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for SUOX located at RS773115 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



## SHMT

The SHMT gene gives your body instructions on how to make the enzyme serine hydroxymethyltransferase. This enzyme helps facilitate the conversion of serine to glycine, and tetrahydrofolate to 5,10-methylene tetrahydrofolate.<sup>53</sup> These reactions support the synthesis of methionine, thymidylate, and purines in the cytoplasm of cells.<sup>53</sup>

The process of converting serine to glycine plays a role in neurotransmitter synthesis, metabolism, and SAMe synthesis.<sup>54</sup> The conversion of serine to glycine helps to shift the emphasis of the methylation cycle away from processing homocysteine, and towards the production of the building blocks needed for new DNA synthesis. SHMT SNPs can interfere with the delicate balance of the methylation cycle, which may result in high levels of homocysteine and depletion of methylation cycle intermediates.

The conversion of tetrahydrofolate to 5,10-methylene tetrahydrofolate plays a role in how folate is broken down in the body, and is critical for cell growth.<sup>55</sup>

Mutations in SHMT have been associated with various diseases, including tumor growth and prognosis, increased DNA damage, and disruptions in folate which result in decreased methylation.<sup>56</sup>

When combined with MTHFR mutations, SHMT SNPs may have a cumulative effect and result in elevated homocysteine levels. Increased homocysteine levels have been associated with cardiovascular disease, stroke, vascular dementia, and Alzheimer's disease.<sup>27,28</sup> These risk factors are related to B vitamin and folate levels in the body.<sup>27,28</sup>

**To find out more about SHMT explore Dr. Amy's book, *Feel Good About Your SNPs*.**

### A NOTE FROM DR. AMY

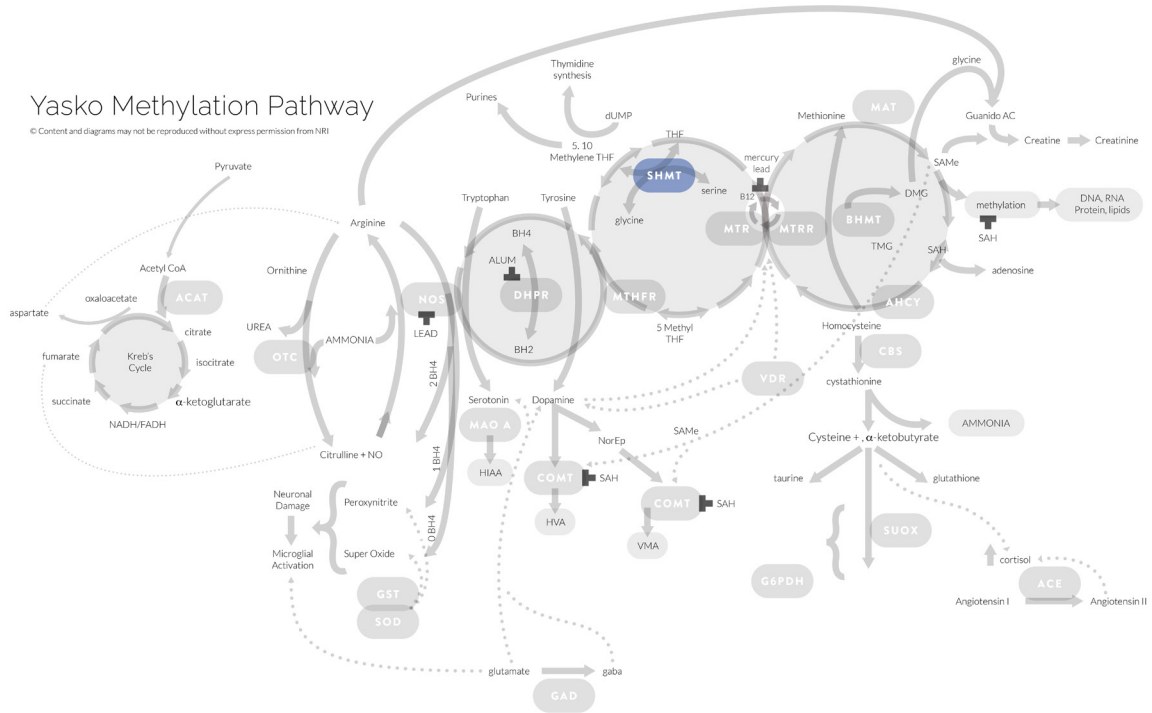
If the methylation cycle is not functioning properly, SHMT can act as a bypass around the pathway to aid in the clearance of (what can be toxic) buildup of high levels of intermediates that are unable to be cleared from the cycle. This is one of the reasons I prefer supplementation with SHMT to support the "short route" of the methylation cycle instead of glycine, trimethylglycine (TMG), or high doses of folinic acid (which can prevent SHMT from functioning properly).



# SHMT

## Yasko Methylation Pathway

© Content and diagrams may not be reproduced without express permission from NRI



SHMT C1420T



TEST RESULT  
VARIATION

**+/+ (MUTATIONS IN BOTH OF YOUR TWO GENES)**  
**C1420T**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Homozygous mutation

*Be sure to work closely with your health care professional for this type of mutation, it's likely you will benefit from extra support on your health journey.*

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

May be more susceptible to iron imbalances in the system, and microbial imbalances in the gut.

Individuals with this mutation may want to monitor their methylation cycle and associated supplementation more closely.

**OPTIMIZE WHAT  
YOU'VE GOT**

Consider supplementation that supports microbial imbalances in the gut, B12 levels, and basic methylation support.

- All In One multivitamin
- DHA
- Folinic acid
- Herbs that support gut imbalances
- Lactoferrin (as needed)
- Phosphatidylserine
- SHMT+ nucleotide blend

**CLICK HERE**

**TO VISIT THE "SNP SUPPORT" HEALTH CATEGORY ON HOLISTICHEAL.COM TO EXPLORE DR. AMY'S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.**

**TRACK YOUR  
PROGRESS**

Use an at-home test kit that measures toxic elements and nutritional elements to assess iron, lithium, and cobalt levels.

Use an at-home test kit that measures amino acids to compare taurine and methionine levels to assess methylation cycle function OR measure homocysteine levels to make sure they're not too high in comparison to s-adenosyl, taurine, and methionine levels.

If iron levels are high, consider a gastrointestinal test to check for the presence of microbial imbalances.





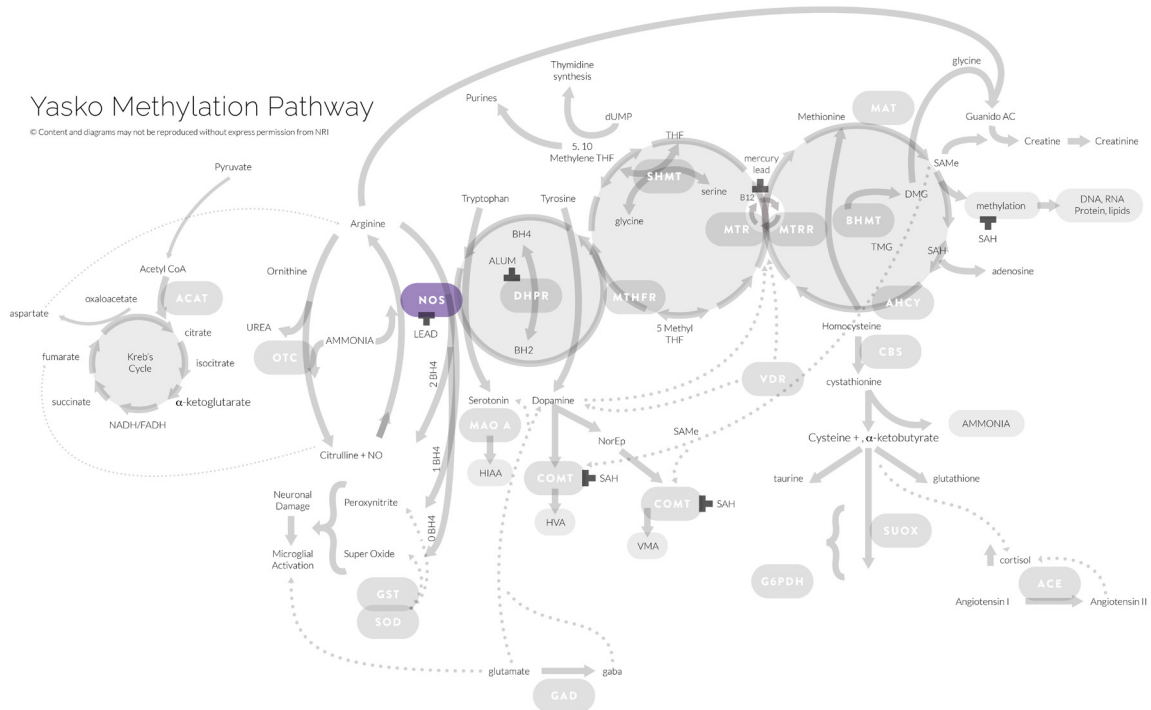
# NOS

The NOS gene gives your body instructions on how to make the enzyme nitric oxide synthase. This enzyme synthesizes nitric oxide from arginine.<sup>57</sup>

Nitric oxide participates in several biologic processes, including neurotransmission and antimicrobial and antitumoral activities.<sup>57,58</sup> It has also been implicated in neurotoxicity associated with stroke and neurodegenerative diseases, smooth muscle relaxation, and blood clotting.<sup>57-59</sup>

The NOS enzyme plays a role in ammonia clearance from the urea cycle, and works in conjunction with BH4.<sup>59,60</sup> BH4 is needed for the production of dopamine and serotonin, which are neurotransmitters associated with mood and attention.<sup>61</sup>

**To find out more about NOS explore Dr. Amy's book, *Feel Good About Your SNPs*.**



NOS D298E



TEST RESULT **-/- (NO MUTATION)**  
VARIATION **NONE (D298E NOT PRESENT)**



**THE YASKO PROTOCOL  
CONSIDERS THIS RESULT**

Normal

**POSSIBLE ASSOCIATED  
HEALTH CONCERNS**

Both genes for NOS located at RS1799983 are functioning optimally for your health!

**OPTIMIZE WHAT  
YOU'VE GOT**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.

**TRACK YOUR  
PROGRESS**

Your genes are functioning optimally for this SNP. There is little to no support needed to maintain your health in this region.



# Ion Transport & ACE

DNA SNP tests detect when a single nucleotide in a DNA sequence is altered. Other DNA mutations can occur, such as insertions or deletions of nucleotides in a DNA sequence, but these changes cannot be assessed by SNP tests.

Although the CFTR gene and ACE gene contain mutations that cannot be detected by DNA SNP tests, Dr. Amy feels they are still important to consider when evaluating personalized supplementation.

The CFTR gene gives your body instructions on how to make the protein cystic fibrosis transmembrane conductance regulator (CFTR).<sup>62</sup> Dr. Amy also refers to this gene as “ion transport.” This protein works as a chloride channel and controls the passage of ion and water secretion and absorption in epithelial tissues.<sup>63</sup> Mutations in this gene can cause cystic fibrosis.<sup>63</sup>

Dr. Amy has noticed that imbalances in ion transport (variations in the CFTR gene) may present as low potassium and lithium levels on tests that measure levels of toxic elements and nutritional elements. These imbalances may also impact GABA levels. Imbalances in ion transport may play a role in apraxia/language development and issues with weight management.

The ACE gene gives your body instructions on how to make angiotensin converting enzyme (ACE).<sup>64</sup> This enzyme is involved in regulating blood pressure and balancing electrolytes in the body.

ACE converts angiotensin I into angiotensin II, and inactivates bradykinin. The ACE enzyme plays a role in male fertility, and mutations in this gene have been associated with cardiovascular disease, psoriasis, renal disease, stroke, and Alzheimer’s disease.<sup>65</sup>

Currently, symptomology that presents as ASD or severe ADHD is the primary indicator for a need to support ion transport and ACE.

If you are interested in assessing the impact that ion transport and the ACE gene may be having on your methylation cycle:

- Consider an at-home test kit that measures levels of toxic elements and nutritional elements to assess lithium, sodium, and potassium levels.
- Use an at-home test kit that monitors levels of lactate and pyruvate to assess ability to convert food into energy and to check for ketones.
- Use an at-home test kit that measures levels of amino acids to check taurine levels in comparison to methionine levels to assess how your methylation cycle is performing OR measure homocysteine levels to make sure they’re not too high in comparison to s-adenosyl, taurine, and methionine levels.
- Work with your health care professional to monitor cholesterol and blood pressure.

**Please Note: If you are on blood pressure medication, take extra care and always consult with your health care professional when using any supplementation to support ACE imbalances.**

[CLICK HERE](#)

TO VISIT THE “SNP SUPPORT” HEALTH CATEGORY ON [HOLISTICHEAL.COM](https://www.holisticheal.com) TO EXPLORE DR. AMY’S HANDPICKED SUPPLEMENTS AND BIOCHEMICAL TESTS FOR THIS SPECIFIC SNP VARIATION.



# References

1. Jin Z, Liu Y. DNA methylation in human diseases. *Genes Dis.* Mar 2018;5(1):1-8. doi:10.1016/j.gendis.2018.01.002
2. P21964 · COMT\_HUMAN. Accessed 04/25/2023. <https://www.uniprot.org/uniprotkb/P21964/entry>
3. COMT catechol-O-methyltransferase [ Homo sapiens (human) ]. Accessed 04/25/2023. <https://www.ncbi.nlm.nih.gov/gene/1312>
4. Qayyum A, Zai CC, Hirata Y, et al. The Role of the Catechol-o-Methyltransferase (COMT) GeneVal158Met in Aggressive Behavior, a Review of Genetic Studies. *Curr Neuropharmacol.* 2015;13(6):802-14. doi:10.2174/1570159x13666150612225836
5. COMT gene catechol-O-methyltransferase. 09/01/2007. Accessed 04/25/2023. <https://medlineplus.gov/genetics/gene/comt/#conditions>
6. Bastos P, Gomes T, Ribeiro L. Catechol-O-Methyltransferase (COMT): An Update on Its Role in Cancer, Neurological and Cardiovascular Diseases. *Rev Physiol Biochem Pharmacol.* 2017;173:1-39. doi:10.1007/112\_2017\_2
7. Nackley AG, Tan KS, Fecho K, Flood P, Diatchenko L, Maixner W. Catechol-O-methyltransferase inhibition increases pain sensitivity through activation of both beta2- and beta3-adrenergic receptors. *Pain.* Apr 2007;128(3):199-208. doi:10.1016/j.pain.2006.09.022
8. VDR vitamin D receptor [ Homo sapiens (human) ]. 04/17/2023. Accessed 04/25/2023. <https://www.ncbi.nlm.nih.gov/gene/7421>
9. VDR gene vitamin D receptor. 12/1/2017. <https://medlineplus.gov/genetics/gene/vdr/>
10. P11473 · VDR\_HUMAN. Accessed 04/25/2023. <https://www.uniprot.org/uniprotkb/P11473/entry>
11. Redenšek S, Kristanc T, Blagus T, Trošt M, Dolžan V. Genetic Variability of the Vitamin D Receptor Affects Susceptibility to Parkinson's Disease and Dopaminergic Treatment Adverse Events. *Front Aging Neurosci.* 2022;14:853277. doi:10.3389/fnagi.2022.853277
12. Lv L, Tan X, Peng X, et al. The relationships of vitamin D, vitamin D receptor gene polymorphisms, and vitamin D supplementation with Parkinson's disease. *Transl Neurodegener.* Sep 01 2020;9(1):34. doi:10.1186/s40035-020-00213-2
13. Swapna N, Vamsi UM, Usha G, Padma T. Risk conferred by FokI polymorphism of vitamin D receptor (VDR) gene for essential hypertension. *Indian J Hum Genet.* Sep 2011;17(3):201-6. doi:10.4103/0971-6866.92104
14. MAOA monoamine oxidase A [ Homo sapiens (human) ]. 04/03/2023. Accessed 04/25/2023. <https://www.ncbi.nlm.nih.gov/gene/4128>
15. Sun X, Ming Q, Zhong X, et al. The MAOA Gene Influences the Neural Response to Psychosocial Stress in the Human Brain. *Front Behav Neurosci.* 2020;14:65. doi:10.3389/fnbeh.2020.00065
16. MAOA gene monoamine oxidase A. 05/01/2017. Accessed 04/25/2023. <https://medlineplus.gov/genetics/gene/maoa/>
17. P24752 · THIL\_HUMAN. Accessed 04/25/2023. <https://www.uniprot.org/uniprotkb/P24752/entry>
18. ACAT1 gene acetyl-CoA acetyltransferase 1. 2020, June 1. <https://medlineplus.gov/genetics/gene/acet1/#conditions>
19. Chang TY, Li BL, Chang CC, Urano Y. Acyl-coenzyme A:cholesterol acyltransferases. *Am J Physiol Endocrinol Metab.* Jul 2009;297(1):E1-9. doi:10.1152/ajpendo.90926.2008
20. MTHFR gene methylenetetrahydrofolate reductase. Accessed 2023, April 25. <https://medlineplus.gov/genetics/gene/mthfr/>
21. P42898 · MTHR\_HUMAN. Accessed 2023, April 25. <https://www.uniprot.org/uniprotkb/P42898/entry>
22. Wan L, Li Y, Zhang Z, Sun Z, He Y, Li R. Methylenetetrahydrofolate reductase and psychiatric diseases. *Transl Psychiatry.* Nov 5 2018;8(1):242. doi:10.1038/s41398-018-0276-6
23. L. D. Methylenetetrahydrofolate Reductase Deficiency. In: Pratt VM SS, Pirmohamed M, et al., editors, ed. *Medical Genetics Summaries* [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2012-; 2012 Mar 8 [Updated 2016 Oct 27].
24. <https://www.ncbi.nlm.nih.gov/gene/4524>. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/4524>
25. MTR gene 5-methyltetrahydrofolate-homocysteine methyltransferase. Accessed 2023, April 25. <https://medlineplus.gov/genetics/gene/mtr/>
26. MTR 5-methyltetrahydrofolate-homocysteine methyltransferase [ Homo sapiens (human) ]. 2023, March 29. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/4548>



27. Ganguly P, Alam SF. Role of homocysteine in the development of cardiovascular disease. *Nutr J*. Jan 10 2015;14:6. doi:10.1186/1475-2891-14-6
28. Seshadri S, Beiser A, Selhub J, et al. Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. *N Engl J Med*. Feb 14 2002;346(7):476-83. doi:10.1056/NEJMoa011613
29. MTRR 5-methyltetrahydrofolate-homocysteine methyltransferase reductase [ Homo sapiens (human) ]. 2023, April 9. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/4552>
30. Q9UBK8 · MTRR\_HUMAN. Accessed 2023, April 25. <https://www.uniprot.org/uniprotkb/Q9UBK8/entry>
31. Q93088 · BHMT1\_HUMAN. Accessed 2023, April 25.
32. Feng Q, Kalari K, Fridley BL, et al. Betaine-homocysteine methyltransferase: human liver genotype-phenotype correlation. *Mol Genet Metab*. Feb 2011;102(2):126-33. doi:10.1016/j.ymgme.2010.10.010
33. BHMT Gene - Betaine--Homocysteine S-Methyltransferase. 2023, March 21. Accessed 2023, April 25. <https://www.genecards.org/cgi-bin/carddisp.pl?gene=BHMT>
34. Wood SK, Valentino RJ. The brain norepinephrine system, stress and cardiovascular vulnerability. *Neurosci Biobehav Rev*. Mar 2017;74(Pt B):393-400. doi:10.1016/j.neubiorev.2016.04.018
35. Biederman J, Spencer T. Attention-deficit/hyperactivity disorder (ADHD) as a noradrenergic disorder. *Biol Psychiatry*. Nov 1 1999;46(9):1234-42. doi:10.1016/s0006-3223(99)00192-4
36. P23526 · SAHH\_HUMAN. Accessed 2023, April 25. <https://www.uniprot.org/uniprotkb/P23526/entry>
37. AHCY adenosylhomocysteinase [ Homo sapiens (human) ]. 2023, April 9. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/191>
38. Vizán P, Di Croce L, Aranda S. Functional and Pathological Roles of AHCY. *Front Cell Dev Biol*. 2021;9:654344. doi:10.3389/fcell.2021.654344
39. P35520 · CBS\_HUMAN. Accessed 2023, April 25. <https://www.uniprot.org/uniprotkb/P35520/entry>
40. CBS cystathionine beta-synthase [ Homo sapiens (human) ]. 2023, April 9. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/875>
41. Fredriksen A, Meyer K, Ueland PM, Vollset SE, Grotmol T, Schneede J. Large-scale population-based metabolic phenotyping of thirteen genetic polymorphisms related to one-carbon metabolism. *Hum Mutat*. Sep 2007;28(9):856-65. doi:10.1002/humu.20522
42. Aras O, Hanson NQ, Yang F, Tsai MY. Influence of 699C->T and 1080C->T polymorphisms of the cystathionine beta-synthase gene on plasma homocysteine levels. *Clin Genet*. Dec 2000;58(6):455-9. doi:10.1034/j.1399-0004.2000.580605.x
43. Kruger WD, Evans AA, Wang L, et al. Polymorphisms in the CBS gene associated with decreased risk of coronary artery disease and increased responsiveness to total homocysteine lowering by folic acid. *Mol Genet Metab*. May 2000;70(1):53-60. doi:10.1006/mgme.2000.2993
44. De Stefano V, Dekou V, Nicaud V, et al. Linkage disequilibrium at the cystathionine beta synthase (CBS) locus and the association between genetic variation at the CBS locus and plasma levels of homocysteine. The Ears II Group. European Atherosclerosis Research Study. *Ann Hum Genet*. Nov 1998;62(Pt 6):481-90. doi:10.1046/j.1469-1809.1998.6260481.x
45. Shan X, Dunbrack RL, Jr., Christopher SA, Kruger WD. Mutations in the regulatory domain of cystathionine beta synthase can functionally suppress patient-derived mutations in cis. *Hum Mol Genet*. Mar 15 2001;10(6):635-43. doi:10.1093/hmg/10.6.635
46. De Lucca M, Casique L. Characterization of cystathionine beta-synthase gene mutations in homocystinuric Venezuelan patients: identification of one novel mutation in exon 6. *Mol Genet Metab*. Mar 2004;81(3):209-15. doi:10.1016/j.ymgme.2003.12.003
47. Janosik M, Kery V, Gaustadnes M, Maclean KN, Kraus JP. Regulation of human cystathionine beta-synthase by S-adenosyl-L-methionine: evidence for two catalytically active conformations involving an autoinhibitory domain in the C-terminal region. *Biochemistry*. Sep 4 2001;40(35):10625-33. doi:10.1021/bi010711p
48. Niu WN, Yadav PK, Adamec J, Banerjee R. S-glutathionylation enhances human cystathionine β-synthase activity under oxidative stress conditions. *Antioxid Redox Signal*. Feb 10 2015;22(5):350-61. doi:10.1089/ars.2014.5891
49. P51687 · SUOX\_HUMAN. Accessed 2023, April 25. <https://www.uniprot.org/uniprotkb/P51687/entry>
50. SUOX sulfite oxidase [ Homo sapiens (human) ]. 2023, March 29. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/6821>
51. Vally H, Misso NL. Adverse reactions to the sulphite additives. *Gastroenterol Hepatol Bed Bench*. Winter 2012;5(1):16-23.
52. SUOX gene sulfite oxidase. 2018, January 1. Accessed 2023, April 25. <https://medlineplus.gov/genetics/gene/suox/#synonyms>



53. SHMT1 serine hydroxymethyltransferase 1 [ Homo sapiens (human) ]. 2023, March 29. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/6470>
54. Razak MA, Begum PS, Viswanath B, Rajagopal S. Multifarious Beneficial Effect of Nonessential Amino Acid, Glycine: A Review. *Oxid Med Cell Longev*. 2017;2017:1716701. doi:10.1155/2017/1716701
55. Menezo Y, Elder K, Clement A, Clement P. Folic Acid, Folinic Acid, 5 Methyl TetraHydroFolate Supplementation for Mutations That Affect Epigenesis through the Folate and One-Carbon Cycles. *Biomolecules*. Jan 24 2022;12(2) doi:10.3390/biom12020197
56. Nonaka H, Nakanishi Y, Kuno S, et al. Design strategy for serine hydroxymethyltransferase probes based on retro-aldol-type reaction. *Nat Commun*. Feb 20 2019;10(1):876. doi:10.1038/s41467-019-08833-7
57. NOS1 nitric oxide synthase 1 [ Homo sapiens (human) ]. 2023, March 29. <https://www.ncbi.nlm.nih.gov/gene/4842>
58. Dawson VL, Dawson TM. Nitric oxide in neurodegeneration. *Prog Brain Res*. 1998;118:215-29. doi:10.1016/s0079-6123(08)63210-0
59. Förstermann U, Sessa WC. Nitric oxide synthases: regulation and function. *Eur Heart J*. Apr 2012;33(7):829-37, 837a-837d. doi:10.1093/eurheartj/ehr304
60. Nagasaka H, Tsukahara H, Yorifuji T, et al. Evaluation of endogenous nitric oxide synthesis in congenital urea cycle enzyme defects. *Metabolism*. Mar 2009;58(3):278-82. doi:10.1016/j.metabol.2008.09.025
61. Fanet H, Capuron L, Castanon N, Calon F, Vancassel S. Tetrahydrobiopterin (BH4) Pathway: From Metabolism to Neuropsychiatry. *Curr Neuropharmacol*. 2021;19(5):591-609. doi:10.2174/1570159x18666200729103529
62. A4L9V0 · A4L9V0\_HUMAN. Accessed 2023, April 25. <https://www.uniprot.org/uniprotkb/P12821/entry>
63. CFTR CF transmembrane conductance regulator [ Homo sapiens (human) ]. 2023, April 20. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/1080>
64. P12821 · ACE\_HUMAN. Accessed 2023, April 25. <https://www.uniprot.org/uniprotkb/P12821/entry>
65. ACE angiotensin I converting enzyme [ Homo sapiens (human) ]. 2023, April 20. Accessed 2023, April 25. <https://www.ncbi.nlm.nih.gov/gene/1636>

