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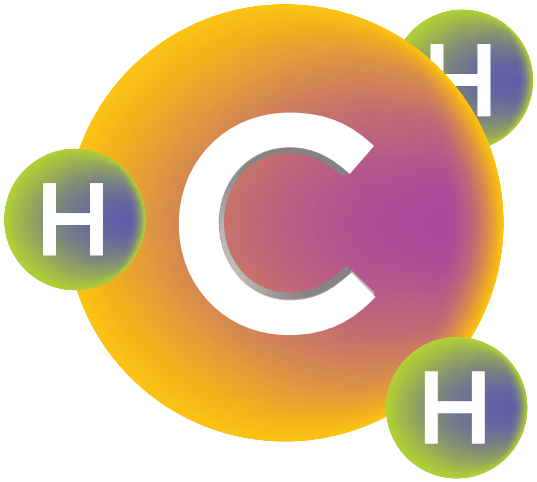
# Comprehensive Methylation Panel with Methylation Pathway Analysis




READ IT. LEARN IT. LIVE IT.

We recommend that you read and understand the Methylation Pathway Analysis and the book Genetic ByPass you received with the test; comprehending the science will enable you to choose the most advantageous regime in order to help you reach and maintain an **optimum level of heath and wellness.**

*With love & hope,*
*Dr. Amy*

# SNP Results and Nutritional Methylation Pathway Analysis

The results of this test should help to put your mind at ease by giving you suggestions that you can actually act on. I only believe in genetic testing if it gives you information that translates into positive constructive action. My personal belief is that genetic testing without any knowledge of how to address issues that are uncovered is unethical. My ultimate goal is to use the Nutrigenomic testing as a guide to proper supplementation to bypass genetic weaknesses that are uncovered by SNP results. The purpose of this MPA or nutritional Methylation Pathway Analysis is to serve as a tool to help you to understand what supplements, herbs and vitamins you can use to bypass weaknesses in a particular nutritional pathway in your body.

While there are a number of other Nutrigenomic tests available on the market, what is special about this test and analysis is that it comprehensively looks at one pathway, what I call the "Methylation Cycle" ("Genetic Bypass", Dr Amy Yasko). I see the Methylation Cycle as the intersection of several important pathways in the body, the common point is a need for "methyl" groups. Methyl groups are simply small chemical compounds whose structure is similar to water. Where water is H2O, a methyl group is CH3. The ability to generate and move these groups is critical to health; these groups are needed for a large number of reactions in the body. "Methylation takes place over billion times a second in the body. It is like one big dance, with bio-chemicals passing methyl groups from one partner to another" (The H Factor, Dr. James Braly and Patrick Holford).

One way to think about the difference between this analysis and others is to think of it in terms of a road map. If you wanted to travel from your hometown to my hometown in Maine you would need a map with detailed directions. This would be especially important if certain roads along the way were closed due to construction, bridges out because of flooding, or other road detours. It would help to have a detailed map drawn for you that took all of these specific situations into account. Your Nutrigenomic test tells you where the "construction" sites are located, which bridges are out and where detours are on your individualized map. With this knowledge you can put together an analysis that will help you get from your hometown to my hometown without getting stuck in a ditch or lost on a detour. The more information you have about specific genes in this particular pathway the easier it is to construct your personal map. This is analogous to having the model of your car, knowing how many miles per gallon you get, how often you feel that you need to stop at a rest area and when you need to fill your tank or take a break from driving. With this information you are in a better position to plan your trip. This is different from other tests that may tell you where your hometown is located and your destination lies on the map, but without any of the specific information between the two points. Without the details, you do not know if the route you may choose has been closed, if the bridge is out, or if there is a detour that will add more time to your travel. Given only a starting and stopping point means the rest of the trip is simply guesswork. The Nutrigenomic test and MPA are designed to take the guesswork out of your trip to health and wellness. While other Nutrigenomic tests look at isolated genes in a wide range of pathways, this test is designed to look comprehensively at a very critical pathway in the body and from that construct a personal road map to health and wellbeing.

Before we get to the specific results of your Nutrigenomic test and the supplement suggestions to help you on your road to health and wellness, it is important to understand that most mutations or SNP variations that are revealed are NOT "all or none mutations". In other words, if you or your loved one has a mutation or a SNP variation, it does not mean that the activity of this gene is completely "off". It may simply mean that it functions at lower efficiency. When you look at the suggested nutritional support, you are working to increase the ability of the entire methylation cycle to run properly, keeping in mind that it has been functioning to some degree in spite of any mutations in particular genes. This is a good opportunity to also explain that a variation or maturation does not always mean a gene is not working at optimal efficiency. Rather, it may sometimes mean that it is working at an increased level. The basic assumption is often made thinking the gene involved is decreased or impaired; however, changes in the DNA sequence can result in an increased activity in the gene. Additionally, changes in the DNA sequence can result in a lack of normal regulation of the gene involved.

Just as the physical location of your hometown and my hometown will not change on a map, your genetics also will not change over time. For this reason this MPA will serve as a road map for your future. Knowledge of your genetics is like having an ultrasound that allows you to see inside of your own individual DNA and to use this information for prevention of potential health issues. Suggestions that are made may be valid today, as well as next week, next year or ten years from now. Once you slowly implement your supplementation, your body can start to support the mutations, this helps in supporting the Methylation Cycle to function properly. This in turn should help your body to detoxify properly.

Unlike genetic tests, biochemical tests will change over time. Biochemical testing measures the amount or activity of a particular enzyme or protein from a sample of urine or stool. Biochemical testing can be used to assess the effect of supplementation on your system. Ideally, the goal is to understand that knowledge is power and knowledge of your genetics, including any mutations, can give you the information you need to make informed decisions on how to supplement and bypass these weaknesses in your system. You can then use biochemical testing (Urine Essential Elements, Urine amino acids, metabolic analysis and urine toxic metal testing) to monitor the progress of your supplementation to bypass your mutations.

You can go to:

http://www.holisticheal.com for more information on biochemical testing.

For those of you who are interested for more in depth information about the Methylation Cycle and the genes involved in this pathway including an understanding of which genes have increased activity, which have regulation problems and those which have reduced activity, I would suggest reading the Genetic Bypass book that you received with your nutrigenomic test kit, or take advantage of the discussion group at http://www.ch3nutrigenomics.com. The following personalized analysis is a streamlined format, designed to help you to make choices about specific supplements to bypass any roadblocks on your way to health but does not contain the detailed information that is in the Genetic Bypass Book.

More information can be found on our following sites:

http://www.holistichealth.com
http://www.knowyourgenetics.com
http://www.recovermychild.com

For anyone with neurological imbalances, I would suggest reading the book

**“The Puzzle of Autism: Putting It all Together”**.

This book has protocols that support detoxification, neurological inflammation, support nerve growth and more; it is not just for autism.

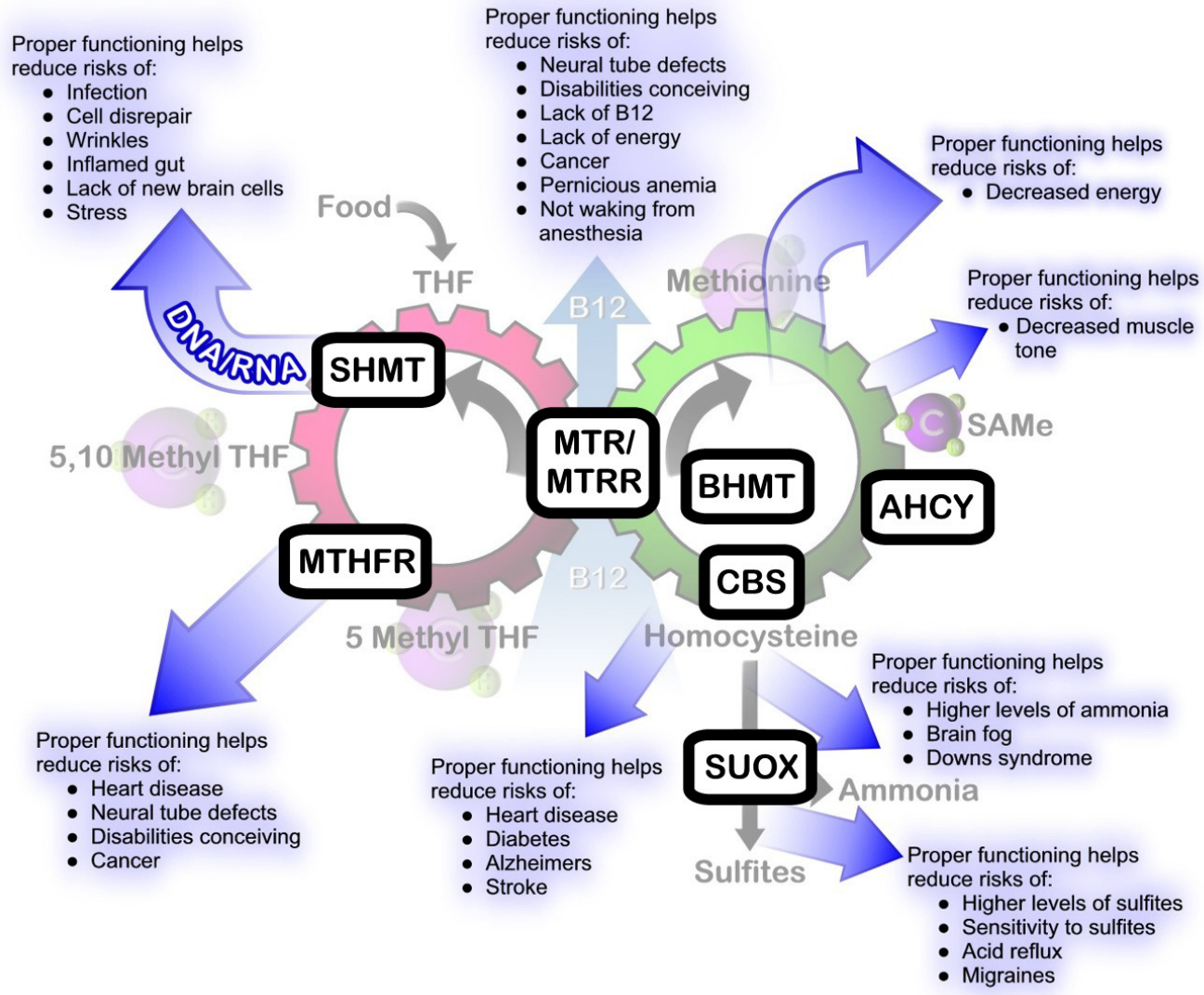
Wishing you good health always,

**Amy Yasko, Ph.D**

# Description Of Genes

The following is a very brief description of the genes that are included in this nutrigenomic panel, including information to help you to understand why it is important to look at nutritional supplementation for any imbalances in the body. Again, for those who would like more detailed and comprehensive information, consider reading **"The Genetic Bypass"** book as well as joining the discussion group at:

www.ch3nutrigenomics.com.



**COMT *(catechol-O-methyltransferase)***:
A primary function of this gene is to help to break down dopamine. Dopamine is a neurotransmitter that is recognized for its role in attention, as well as reward seeking behavior. Dopamine helps to cause pleasurable feelings that aid in reinforcing positive behaviors and motivating individuals to function in certain reward gaining activities. COMT is also involved in the breakdown of another neurotransmitter, norepinephrine. The balance between norepinephrine levels and dopamine levels has been implicated in ADD/ADHD; in addition, dopamine levels are important in conditions such as Parkinson's disease. COMT is also involved in the proper processing of estrogen in the body. Sensitivity to pain has recently been found to be correlated with COMT activity, such that COMT + + individuals may be more sensitive to pain.

**VDR/Taq and VDR/Fok *(vitamin D receptor)***:
The panel looks at more than one portion of the vitamin D receptor, the Taq as well as the Fok sites. While the Fok change has been related to blood suMPA regulation, changes at Taq can affect dopamine levels. For this reason it is important to look at the composite of the COMT and VDR/Taq status and make supplement suggestions based on the combined results at these two sites. The focus on changes in the Fok portion of the VDR is in reMPAd to supplements that support the pancreas and aid in keeping blood suMPA in the normal healthy range.

**MAO A *(monamine oxidase A)***:
MaoA is involved in the breakdown of serotonin in the body. Like dopamine, serotonin is another neurotransmitter in the body. It is involved with mood, and imbalances in serotonin levels have been associated with depression, aggression, anxiety and OCD behavior. Since Mao A is inherited with the X chromosome and is considered a dependent trait it may not show standard inheritance characteristics in males. Since the X chromosome in males can only come from the mother, this means that the fathers Mao A mutations (or lack there of) does not play a role in their son's Mao A status. For females, since one X chromosome is inherited from each parent, the genetics tend to reflect the Mao A status of both parents.

**ACAT *(acetyl coenzyme A acetyltransferase)***:
ACAT plays a role in cholesterol and other lipid balance in the body, helping to prevent the accumulation of excess cholesterol in certain parts of the cells in the body. ACAT is also involved in energy generation in the body. It is involved in helping to allow protein, fats and carbohydrates from food to be converted into an energy form that can be used by your body. In addition, lack of ACAT may also cause a depletion of B12, which is needed for the "long route" around the methylation cycle.

**ACE *(angiotensin converting enzyme)***:
Changes can occur that affect the activity of the ACE gene that can lead to elevated blood pressure. In animal studies imbalances in this pathway were also correlated with increased anxiety and decreases in learning and memory. Increased ACE activity can also throw off the essential mineral balance in the your system due to decreased excretion of sodium in the urine and increased excretion of potassium in the urine. This reaction is also tied to the stress response such that situations of

chronic stress can result in additional sodium retention and increased potassium excretion. This excess potassium is excreted provided that the kidneys are functioning properly. In the event that kidney function is compromised, it can lead to the retention of potassium in the body. ACE is a deletion, it is not a SNP. As a consequence it does not associate in the same manner that the other single nucleotide polymorphisms (SNP) on this panel do, so the inheritance pattern of the ACE deletion may not distribute in the same manner as single base changes.

**MTHFR *(methylenetetrahydrofolate reductase)***:
The MTHFR gene product is at a critical point in the methylation cycle. It helps to pull homocysteine into the cycle, serving to aid in keeping the levels in a normal healthy range. Several mutations in the MTHFR gene have been well characterized as increasing the risk of heart disease, as well as cancer, and may play a role in the level of the neurotransmitters serotonin and dopamine.

**MTR/MTRR *(methionine synthase/ methionine synthase reductase)***:
These two gene products work together to regenerate and utilize B12 for the critical "long way" around the methylation pathway, helping to convert homocysteine to methionine. High levels of homocysteine have been implicated as risk factors in a number of health conditions including heart disease as well as Alzheimer's disease. As is the case for COMT and VDR Bsm/Taq, the MTR and MTRR composite status is also important. Mutations in MTR can increase the activity of this gene product so that it leads to a greater need for B12 as the enzyme is using up B12 at a faster rate. The MTRR helps to recycle B12 for use by the MTR. Mutations that affect its activity would also suggest a greater need for B12.

**BHMT *(betaine homocysteine methyltransferase)***:
The product of this gene is central to the "short cut" through the methylation cycle, again helping to convert homocysteine to methionine. The activity of this gene product can be affected by stress, by cortisol levels and may play a role in ADD/ADHD by affecting norepinephrine levels.

**AHCY 1,2,19 (*S adenosylhomocysteine hydrolase)*:**
AHCY is the enzyme that converts s adenosyl homocysteine (SAH) to adenosine and homocysteine. Decreased AHCY activity should lead to lower levels of homocysteine. Studies using animals with no CBS function suggests that the relationship between CBS enzyme activity, homocysteine levels and SAH and SAMe levels may not be as simple or predictable as one might expect from pathway diagrams. In addition, both SAH and SAMe have been found to affect CBS activity and SAH is known to inhibit methyltrasferase reactions. Also the level of homocysteine affects SAH levels such that higher levels of homocysteine can increase SAH. Clearly, the relationship between these intermediates appears to be complex. (PNAS 2008, 103:17; Theorectic Biology and Medical Modelling 2008, 5:8; JBC 2002, 277:41; Jnutrition 2002,132) It may be especially important for those with AHCY mutations to monitor amino acid levels in order to balance the effects of AHCY mutations, CBS up regulations and other methylation cycle mutation on the system.

**CBS *(cystathionine-beta-synthase)***:
The CBS enzyme basically acts as a gate between homocysteine and the downstream portion of the pathway that generates ammonia in the body. The types of CBS mutations that are identified on this SNP panel cause this "CBS gate" to be left open, this "open gate" is not a neutral situation. The "open gate" can allow support that is added for the rest of the methylation pathway to be depleted,

including any B12 that is used to address MTR and MTRR mutations. While there are some positive end products that are generated via the downstream portion of the pathway such as glutathione and taurine, there are also negative byproducts such as excess ammonia and sulfites. By virtue of increased CBS activity, these sulfur groups that were complexed as part of the methylation cycle can now be released into the system as sulfites which are toxic to the body and put an additional burden on the SUOX gene product.

**SUOX *(sulfite oxidase)***:
This gene product helps to detoxify sulfites in the body. Sulfites are generated as a natural byproduct of the methylation cycle as well as ingested from foods we eat. Sulfites are sulfur based preservatives that are used to prevent or reduce discoloration of light-colored fruits and vegetables, prevent black spots on shrimp and lobster, inhibit the growth of microorganisms in fermented foods such as wine, condition dough, and maintain the stability and potency of certain medications. Sulfites can also be used to bleach food starches, to prevent rust and scale in boiler water that is used to steam food, and even in the production of cellophane for food packaging. The Food and Drug Administration estimates that one out of a hundred people is sulfite-sensitive, and five percent of those also suffer from asthma. A person can develop sulfite sensitivity at any point in life. Because many reactions have been reported, the FDA requires the presence of sulfites in processed foods to be declared on the label. Scientists have not pinpointed the smallest concentration of sulfites needed to trigger a reaction in a sulfite-sensitive person. Difficulty in breathing is the most common symptom reported by sulfite-sensitive people. Sulfites give off the gas sulfur dioxide, which can cause irritation in the lungs, and cause a severe asthma attack for those who suffer from asthma. Responses in the sulfite-sensitive person can vary. Sulfites can cause chest tightness, nausea, hives and in rare cases more severe allergic reactions. Mutations in SUOX may be a risk factor for certain types of cancer, including leukemia.

**SHMT *(serine hydroxymethyltransferase)***:
This gene product helps to shift the emphasis of the methylation cycle toward the building blocks needed for new DNA synthesis and way from the processing of homocyteine to methionine. While DNA building blocks are important, mutations which affect the ability to regulate this gene product and interfere with the delicate balance of the methylation cycle may cause accumulations in homocysteine as well as imbalances in other intermediates in the body.

**NOS *(nitric oxide synthase)***: The NOS enzyme plays a role in ammonia detoxification as part of the urea cycle. Individuals who are NOS + + have reduced activity of this enzyme. NOS mutations can have additive effects with CBS up regulations due to the increased ammonia that is generated by the CBS up regulations.

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The following page has the results of your test. The following is a guide to use.

**Minus “-” represents no mutation**

**Plus “+” represents a mutation**

**“-/-” indicates there is no mutation.**

**“+/-” indicates there is one mutation.**

**“+/+” indicates there is a double mutation.**

Please note: The results column is color coded to correspond with the level of the support needed as listed in the suggested supplementation section of the MPA.

| Gene Name | Variation | Result | Call |
|---|---|---|---|
| COMT | V158M | +/- | Hetero |
| COMT | H62H | +/- | Hetero |
| COMT | 61 | -/- | G |
| VDR | Taq | +/+ | T |
| VDR | Fok | -/- | C |
| MAO A | R297R | +/+ | T |
| ACAT | 1-02 | -/- | G |
| ACE | Del16 | +/+ | DELETION |
| MTHFR | C677T | +/- | Hetero |
| MTHFR | 3 | -/- | C |
| MTHFR | A1298C | +/- | Hetero |
| MTR | A2756G | -/- | A |
| MTRR | A66G | +/- | Hetero |
| MTRR | H595Y | -/- | C |
| MTRR | K350A | -/- | A |
| MTRR | R415T | -/- | C |
| MTRR | S257T | -/- | T |
| MTRR | 11 | -/- | G |
| BHMT | 1 | +/- | Hetero |
| BHMT | 2 | +/- | Hetero |
| BHMT | 4 | +/- | Hetero |
| BHMT | 8 | +/- | Hetero |
| AHCY | 1 | +/- | Hetero |
| AHCY | 2 | +/- | Hetero |
| AHCY | 19 | +/- | Hetero |
| CBS | C699T | +/- | Hetero |
| CBS | A360A | +/- | Hetero |
| SUOX | S370S | -/- | No Support Needed |
| SHMT | C1420T | +/- | Hetero |
| NOS | D298E | -/- | G |

**Suggested supplementation for consideration based on John Doe personal SNP results:**

Please note: If a supplement is listed for more than one mutation, please take only one recommended dose of that supplement.

**Basic Methylation Cycle For All SNPs**

- ☐ 2 - 3 Neurological Health Formula (HHI General Vitamin) or equivalent
- ☐ 1/4 FolaPro
- ☐ 1/4 Intrinsi B12/Folate
- ☐ 1 Nucleotide mix daily (Nucleotide Immune Support)
- ☐ 1 PS/PE/PC (Phosphatidyl Serine Complex)
- ☐ 1 - 2 Hydroxycobalamin B12 Chewable
- ☐ Oral Hydroxy B12 spray (GET-B12)
- ☐ 1x / day Methylation Support RNA
- ☐ at least 1x / week Kidney Support RNA
- ☐ at least 1x / week Organ RNA

**COMT V158M (COMT H62H) +/- VDR/Taq +/+**

- ☐ COMT V158M + - Mutation Specific Formula RNA
- ☐ VDR Taq + Mutation Specific Formula RNA
- ☐ 2 Hydroxycobalamin B12 Chewable
- ☐ PS/PE/PC (Phosphatidyl Serine Complex)
- ☐ Oral Hydroxy B12 spray (GET-B12)
- ☐ 1 Sage
- ☐ 1 Rosemary
- ☐ 1 Vitamin D
- ☐ 1 SAMe
- ☐ 1/2 Curcumin
- ☐ 1/2 Quercetin

**MAO A +/+**

- ☐ MAO A + Mutation Specific Formula RNA
- ☐ Low dose Mood S Formula RNA, very frequent dosing of very small amounts
- ☐ Low dose 5HTP (HTP5 Optimum Mood Support), very frequent dosing of very small amounts
- ☐ 1 Niacinamide
- ☐ 1 NADH
- ☐ Low dose St. Johns Wort, very frequent dosing of very small amounts

**ACE +/+**

- ☐ ACE + Mutation Specific Formula RNA
- ☐ Low dose Anxiety Balancing RNA
- ☐ 1/2 OraKidney
- ☐ 1/2 OraAdrenal (Ora-Adren-80)
- ☐ Low dose Stress Foundation RNA

☐ Low dose Kidney Support RNA
☐ Low dose Progesterone Cream (Pro-Gest Cream)

**MTHFR C677T +/-**

☐ MTHFR C677T + Mutation Specific Formula RNA
☐ 1/4 FolaPro
☐ 1/4 Intrinsi B12/Folate
☐ 1/2 to 1 Nucleotide mix daily (Nucleotide Immune Support)
☐ 1 - 2x / day PS/PE/PC (Phosphatidyl Serine Complex)
☐ 1 Hydroxycobalamin B12
☐ 1 Adenosyl B12 (Dibencozide), daily
☐ 1/2 Vitamin E Succinate
☐ B12 Patch
☐ Oral Hydroxycobalamin (Hydroxo-12 B12 Drops)
☐ Oral Hydroxy B12 spray (GET-B12)
☐ Neurological Health Formula (HHI General Vitamin) or equivalent
☐ 1/8 Actifolate, after 8 weeks support
☐ 1/8 Folic Acid, after 8 weeks support

**MTHFR A1298C +/-**

☐ MTHFR A1298C + Mutation Specific Formula RNA
☐ Low dose BH4 or BioOrgan
☐ NADH
☐ 1/4 FolaPro

**MTRR A66G +/-**

☐ MTR/MTRR + Mutation Specific Formula RNA
☐ 1/4 FolaPro
☐ 1/4 Intrinsi B12/Folate
☐ 1/2 to 1 Nucleotide mix daily (Nucleotide Immune Support)
☐ 1 - 2x / day PS/PE/PC (Phosphatidyl Serine Complex)
☐ 1 Hydroxycobalamin B12
☐ 1 Adenosyl B12 (Dibencozide), daily
☐ 1/2 Vitamin E Succinate
☐ B12 Patch
☐ Oral Hydroxycobalamin (Hydroxo-12 B12 Drops)
☐ Oral Hydroxy B12 spray (GET-B12)
☐ Neurological Health Formula (HHI General Vitamin) or equivalent
☐ 1/8 Actifolate, add after 8 weeks support
☐ 1/8 Folic Acid, add after 8 weeks support

**BHMT 1 +/-**

☐ BHMT 1,2,4 + Mutation Specific Formula RNA

- ☐ Low dose Ammonia Support RNA
- ☐ Stress Foundation RNA
- ☐ Limit Taurine
- ☐ 1 L-Carnitine
- ☐ 1 Policosanol
- ☐ 1 Cholacol
- ☐ 1 GSH Caps
- ☐ 1/2 SAMe
- ☐ 1/2 to 1 Curcumin

**BHMT 2 +/-**

- ☐ BHMT 1,2,4 + Mutation Specific Formula RNA
- ☐ Low dose Ammonia Support RNA
- ☐ Stress Foundation RNA
- ☐ Limit Taurine
- ☐ 1 L-Carnitine
- ☐ 1 Policosanol
- ☐ 1 Cholacol
- ☐ 1 GSH Caps
- ☐ 1/2 SAMe
- ☐ 1/2 to 1 Curcumin

**BHMT 4 +/-**

- ☐ BHMT 1,2,4 + Mutation Specific Formula RNA
- ☐ Low dose Ammonia Support RNA
- ☐ 1/2 to 1 Curcumin
- ☐ 1/2 SAMe
- ☐ 1 GSH Caps
- ☐ 1 to 2 Cholacol
- ☐ 1 Policosanol
- ☐ 1 L-Carnitine
- ☐ 1 Lactoferrin
- ☐ 1 Nucleotide mix daily (Nucleotide Immune Support)
- ☐ Limit Taurine
- ☐ Stress Foundation RNA
- ☐ Pig Duodenal Substance
- ☐ 1 to 2 CCK (Resist Fat Apex Lean)
- ☐ 1 - 2 OraPancreas
- ☐ Super Digestive Enzymes (Enhanced), with each meal

**BHMT 8 +/-**

- ☐ BHMT 8 + Mutation Specific Formula RNA
- ☐ Low dose Attention Support RNA

- ☐ NADH
- ☐ 1 DMG (dimethyl glycine)
- ☐ 2 Hydroxycobalamin B12 Chewable
- ☐ Stress Foundation RNA

**AHCY 1 +/-**

- ☐ AHCY + Mutation Specific Formula RNA
- ☐ 2 to 3 Nucleotides (Nucleotide Immune Support)
- ☐ Low dose Apraxia Support RNA
- ☐ NADH
- ☐ 1X/day Bowel Support Plus RNA
- ☐ Stomach pH Balancing RNA, daily
- ☐ Immunfactor 5
- ☐ Low dose Serenaid

**AHCY 2 +/-**

- ☐ AHCY + Mutation Specific Formula RNA
- ☐ 2 to 3 Nucleotides (Nucleotide Immune Support)
- ☐ Low dose Apraxia Support RNA
- ☐ NADH
- ☐ 1X/day Bowel Support Plus RNA
- ☐ Stomach pH Balancing RNA, daily
- ☐ Immunfactor 5
- ☐ Low dose Serenaid

**AHCY 19 +/-**

- ☐ AHCY + Mutation Specific Formula RNA
- ☐ 2 to 3 Nucleotides (Nucleotide Immune Support)
- ☐ Low dose Apraxia Support RNA
- ☐ NADH
- ☐ 1X/Day Bowel Support Plus RNA
- ☐ Stomach pH Balancing RNA, daily
- ☐ Immunfactor 5
- ☐ Low dose Serenaid

**CBS C699T +/- CBS A360A +/-**

- ☐ Twice day CBS + Mutation Specific Formula RNA and/or Ammonia Support Formula RNA, (before using both check Taurine levels on UAA)
- ☐ Low protein Diet
- ☐ Yucca, on high protein foods
- ☐ Limit Sulfur and limited B6 (or P5P)
- ☐ 1 OraKidney
- ☐ 1x / week Charcoal/Magnesium Flush (Activated Charcoal/Magnesium Citrate flushes)

☐ 1 Hydroxycobalamin B12 Chewable

**SHMT +/-**

☐ SHMT + Mutation Specific Formula RNA
☐ 1/8 Actifolate
☐ 1 Lactoferrin
☐ 1 Nucleotide mix daily (Nucleotide Immune Support)
☐ 1/2 to 1 IP6 (Inositol Hexaphosphate)

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