Your SIMPLIFIED Road Map to Health

What is the difference between this SIMPLIFIED road map and the MPA?

The **MPA (Methylation Pathway Analysis)** is a more detailed explanation of each of the SNPS on Dr. Yasko's Methylation SNP panel, and is designed for a more comprehensive commitment to the program. Dr. Amy has found that there are some individuals who do not have the time to approach the program and fully customize it. Thus the **SIMPLIFIED** road map still takes into account the nutrigenomic profile and SNPs but does so in a more streamlined fashion. It has fewer intricacies and caveats so that it is easier to comply with the program, although you lose some of the customization in choosing a more streamlined approach. The **SIMPLIFIED** road map should still enable you to get a sense of supplement choices to bypass SNPs that were identified by any test.

Since some individuals may be following this **SIMPLIFIED** road map that have run other SNP tests, please be aware that Dr. Yasko cannot be held responsible for results from other SNP tests. It is up to the user to take responsibility for results of any SNP test that are used to make supplement determinations. As always you do want to work with and defer to your doctor for any supplement program. Please review the disclaimer below. In following the suggestions in this **SIMPLIFIED** road map you agree to the terms of the disclaimer.

I look forward to helping as many of you as possible on your personal road map to health!!
With love and hope, Dr. Amy

This Simplified Protocol is dedicated to the memory of Dr. Rich Van Konynenburg, Ph.D., who worked tirelessly to provide a version of this program to help adults with Chronic Fatigue Syndrome (CFS).

What makes Dr. Amy Yasko's protocol different?

Dr. Amy's protocol takes into account that each of us is unique and a one size fits all approach to health is not the answer. This program was designed by Dr. Amy Yasko, with a background in both integrative healthcare as well as more traditional training. This program has been successfully used to help support complex health conditions such as autism and chronic fatigue syndrome. Now, this **simplified version** of the same basic health program is available to help customize each individual's personal roadmap to health. This program takes into account genetic weaknesses as well as the role played by the environment and infectious agents in developing a tailored plan to keep you on the road to health.

Your individualized roadmap

It has been Dr. Yasko's experience that most health conditions in society today are *multifactorial conditions,* meaning that a number of circumstances need to go awry simultaneously for nonideal health to manifest. Multifactorial conditions stem from underlying genetic susceptibility combined with assaults from environmental stressors and infectious agents. Basic parameters like age and gender, along with other genetic and environmental factors play a role in the onset of non-ideal health. Infections combined with excessive environmental burdens will generally only lead to problems with health if they occur in individuals with the *appropriate genetic susceptibility*.

Personalized nutrigenomic screening

One clear, definitive way to evaluate the genetic contribution of multifactorial conditions is to take advantage of new methodologies that allow for personalized genetic screening. Currently, tests are available to identify a number of underlying genetic changes in an individuals' DNA.

The field of **nutrigenomics** is the study of how natural products and supplements can interact with particular genes to decrease the risk of disease. By looking at changes in the DNA in these nutritional pathways it enables one to make supplement choices based on their particular genetics, rather than using the same support for every individual regardless of their unique needs. A knowledge of imbalances in nutritional genetic pathways allows one to utilize combinations of nutrients, foods and natural ribonucleic acids to bypass mutations and restore proper pathway function.

The *methylation cycle* is a central pathway in the body that is particularly amenable to nutrigenomic screening for genetic weaknesses. The result of decreased activity in this pathway causes a shortage of critical functional groups in the body called *methyl groups* that serve a variety of important functions.

Your body's personal mechanic

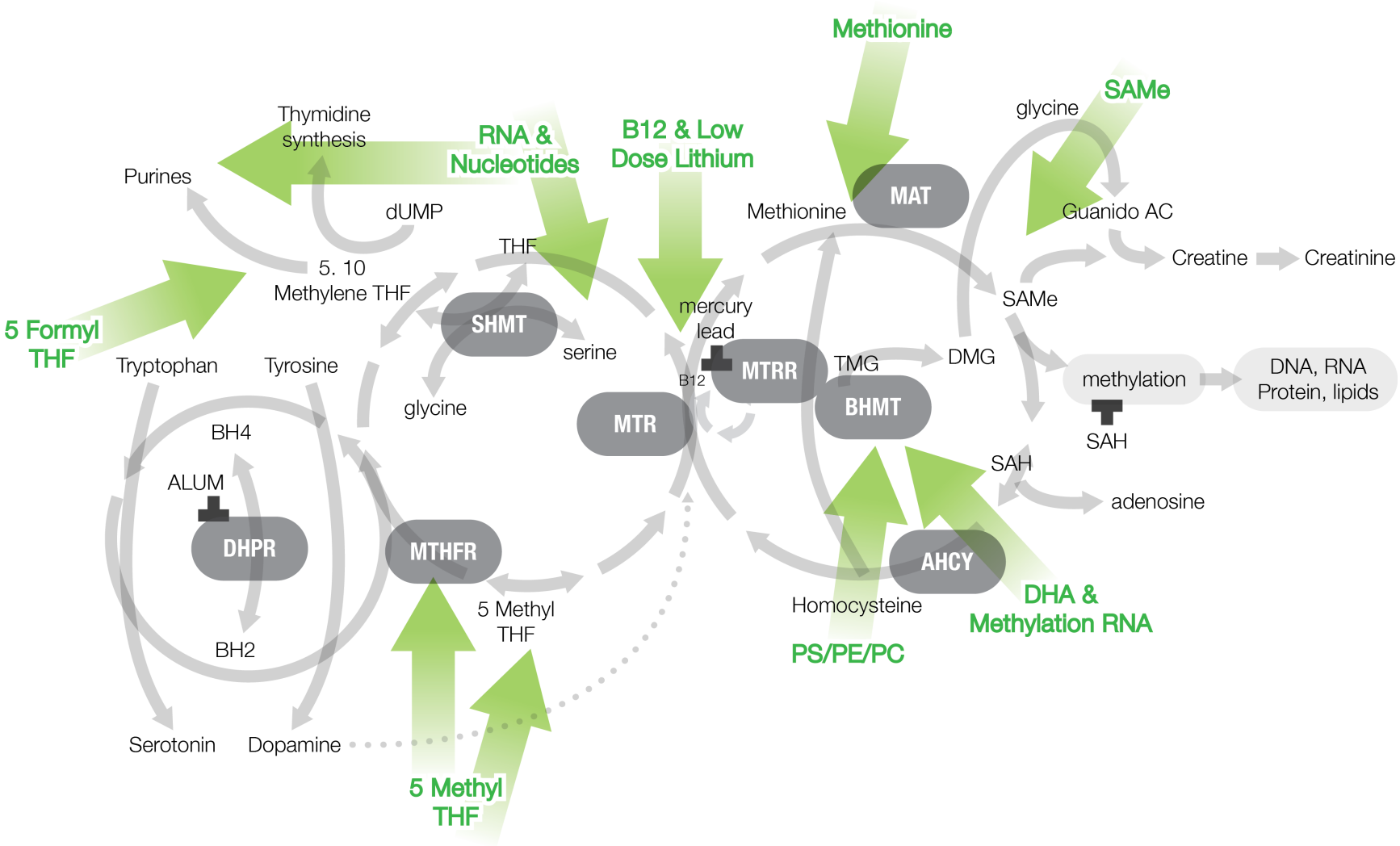
While the term may seem intimidating, a *methyl* group is actually just a group of small molecules, similar in size to the water molecule (H2O). Water is a key to life as are methyl groups critical for health and wellbeing. Methyl groups are simply "CH3" groups; they contain 'H' like in water and a 'C' like in coal or diamonds. However, these very basic molecules serve integral functions; they are moved around in the body to turn on or off genes.

One way to look at the role of methyl groups is that they serve as your own personal *mechanic* for your body, helping to repair and direct functions in your body. If we think about your body like a car then let's assume that you have just one car that you need to maintain over the course of your life, with the help of your own personal *mechanic.* The longer you have that car the more outdated it will become. Over the course of a lifetime the car body will accumulate rust and can rot out. Tires may wear out, the engine may need an overhaul. Alternatively the problems may be simpler such as the need for more wiper fluid or simply to keep the car filled with gas and to change the oil. In any case your personal *mechanic* ensures that your car keeps running, that it can stay on the road…in this case on the road to health. If however your mechanic is unable to function, then all of these issues will start to accumulate over the course of the lifetime of your car. The rust may get so bad that car components fall off like your muffler or the tires become so worn that it is impossible to navigate a turn without the fear of blowing a tire. In the absence of your *mechanics* function you have no way to repair all of the large and small problems that arise with your car to the point where your car can no longer function.

You can start to see why the proper functioning of the pathway that serves to direct your genes is so important. In addition to the editing of genes, this pathway also serves more direct roles in your body and is thus critical for overall health. While there are several particular sites in this pathway where blocks can occur as a result of genetic weaknesses, thankfully supplementation with appropriate foods and nutrients can help to bypass these mutations to allow for restored function of this pathway.

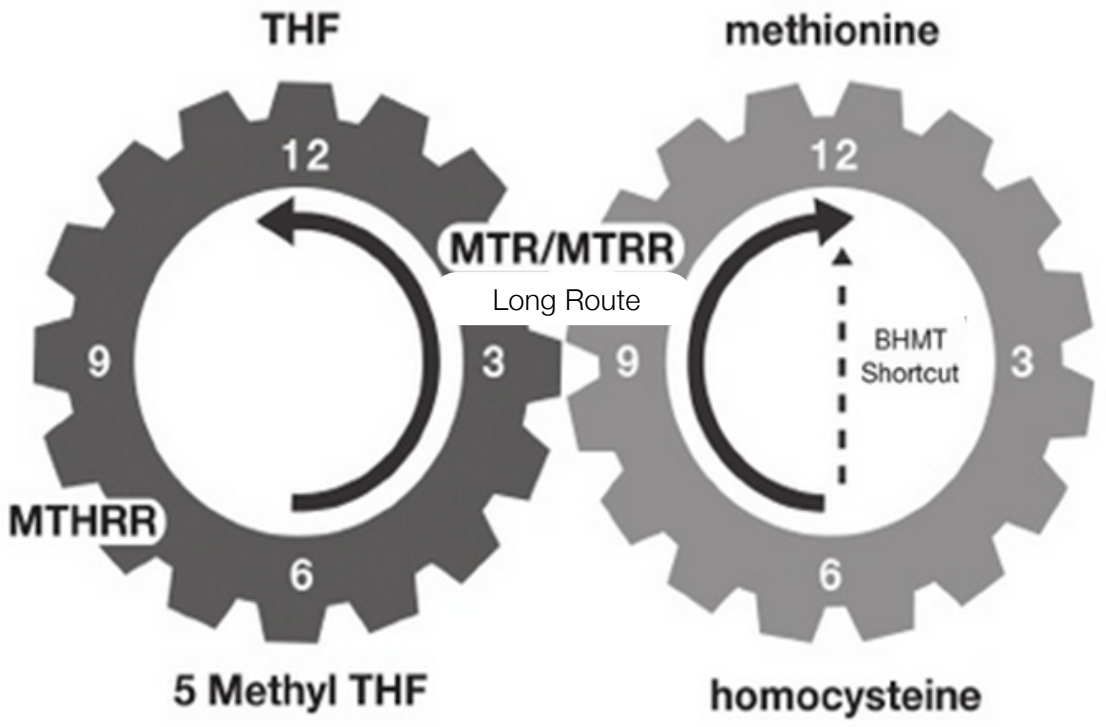
By testing to look at mutations in the DNA for this methylation cycle it is possible to draw a personalized map for each individual's imbalances which may impact upon their health. Once the precise areas of genetic fragility have been identified, it is then possible to target appropriate nutritional supplementation of these pathways to optimize the functioning of these crucial biochemical processes. As seen in the ***diagram*** below there are specific places in the cycle where support can be added. This support helps to bypass mutations in the pathway in a similar manner to the way you might take a detour on a highway. We can look at mutations in this pathway as analogous to a collision that has totally shut down traffic going in one direction on a highway. Support to bypass mutations in this pathway is like taking an alternate route to avoid the accident on the highway. Thus, the use of key nutrients or foods can aid in helping to bypass methylation cycle mutations and help restore function to this pathway

As always work with and defer to your doctor

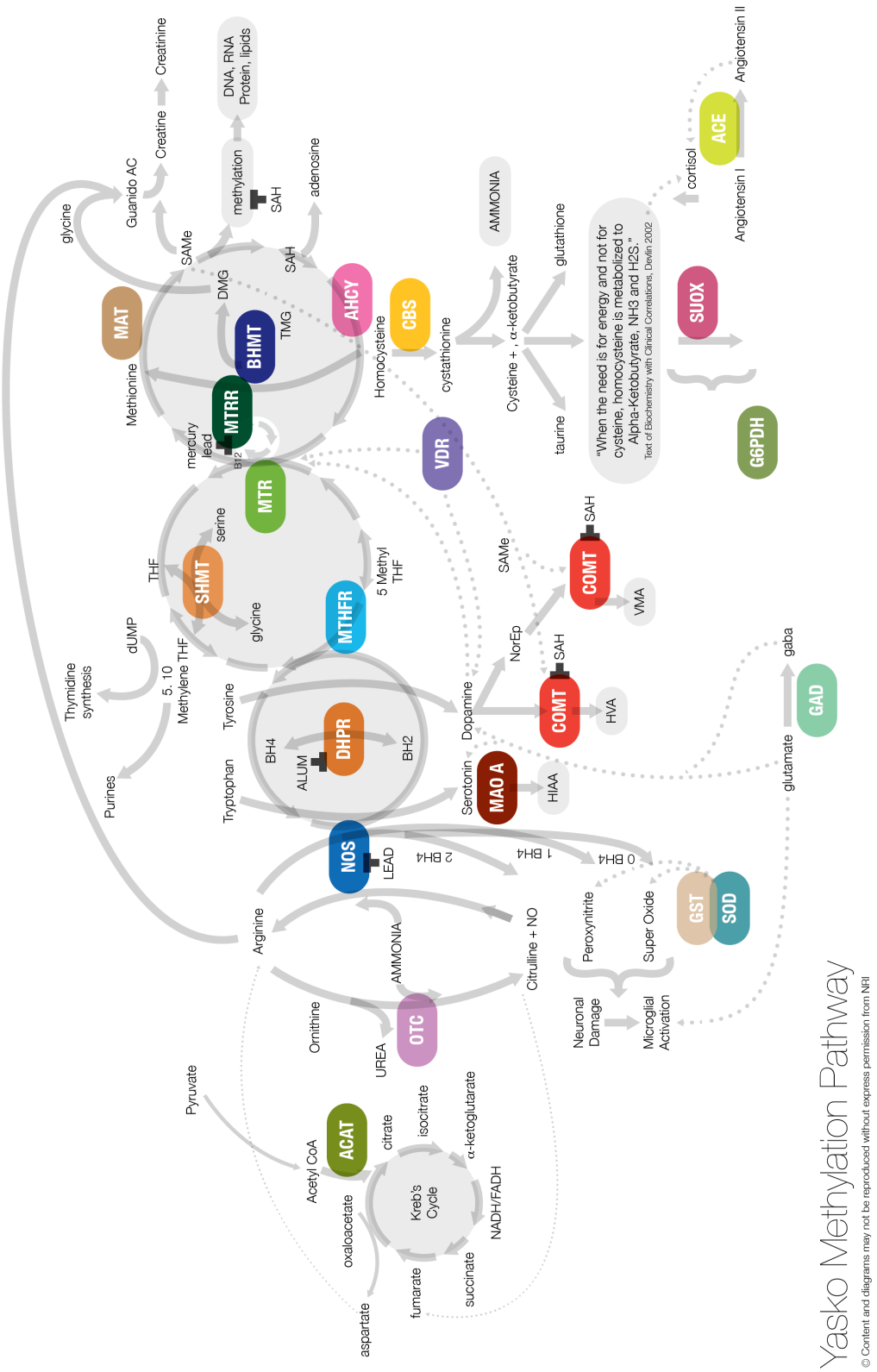


Dr. Amy Yasko looks at two routes around the methylation cycle: the short cut through BHMT and the long route around the cycle via MTR/MTRR and B12. While the ultimate goal is to support healthy function though both routes around the cycle, initially Dr. Amy focuses on short cut support. Then, long route support is layered in for more complete methylation cycle support.

Long route and Short Cut around the cycle:



Complete Methylation Cycle:



The Methylation Cycle is the intersection of several important pathways in the body; the common point is the need for methyl groups. Recall that methyl groups are simply small chemical compounds whose structure is similar to water. 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 a billion times a second in the body. It is like one big dance, with biochemicals passing methyl groups from one partner to another." (The H Factor, Dr.James Brady and Patrick Holford).

The role of the methylation cycle in your body

The methylation cycle is the ideal pathway to focus on for nutritional genetic analysis because the places where mutations occur is well defined and it is clear where supplements can be added to bypass these mutations. In addition to its editing role, the function of this pathway is essential for a number of critical reactions in the body. One consequence of genetic weaknesses (mutations) in this pathway is increased risk factors for a number of serious health conditions. Defects in methylation lay the appropriate groundwork for the further assault of environmental and infectious agents resulting in a wide range of conditions including 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.

- **Inflammation, bacterial and viral infection**

When you have bacterial or viral infections in your system it increases the level of inflammation in your body. Chronic inflammation would therefore exacerbate existing genetic mutations in this same pathway. The inability to progress normally through the methylation pathway as a result of methylation cycle mutations combined with the impact of viral and bacterial infections further compromises the function of this critical system in the body.

- **New cells and the immune system**

The building blocks for DNA and RNA require the methylation pathway to function optimally. Without adequate DNA and RNA it is difficult for the body to synthesize new cells. New cell synthesis is needed to repair damaged cells, to maintain the lining of the gut, to make new blood cells as well as for your immune system that defends you against infection.

T cells are a key aspect of your immune system and they require new DNA in order to respond to foreign invaders. T cell synthesis is necessary to respond to bacterial, parasitic and viral infection, as well as for other aspects of the proper functioning of the immune system.

- **Herpes, hepatitis and other viruses**

In addition, decreased levels of methylation can result in improper DNA regulation. DNA methylation is necessary to prevent the expression of viral genes that have been inserted into the body's DNA. Loss of methylation can lead to the expression of inserted viral genes such as herpes and hepatitis among other viruses.

- **Sensory overload**

Proper levels of methylation are also directly related to the body's ability to both myelinate nerves and to prune nerves. Myelin is a sheath that wraps around the nerve to insulate and facilitate proper nerve reaction. Without adequate methylation, the nerves cannot myelinate in the first place, or cannot remyelinate after insults such as viral infection or heavy metal toxicity. A secondary effect of a lack of methylation and hence decreased myelination is inadequate pruning of nerves. Pruning helps to prevent excessive wiring of unused neural connections and reduces the synaptic density. Without adequate pruning the brain cell connections are misdirected and proliferate into dense, bunched thickets. When nerves grow in this unregulated fashion it can cause confusion processing signals. *Synesthesia* occurs when the stimulation of one sense causes the involuntary reaction of other senses, basically sensory overload.

- **Serotonin, dopamine and ADD/ADHD**

Methylation is also directly related to substances in your body that affect your mood and neurotransmitter levels of both serotonin and dopamine. In addition to its direct role as a neurotransmitter, dopamine is involved in assuring your cell membranes are fluid and have mobility. This methylation of phospholipids in the cell membranes has been related to ADD/ADHD. Membrane fluidity is also important for a variety of functions including proper signaling of the immune system as well as protecting nerves from damage. A number of serious neurological conditions cite reduced membrane fluidity as part of the disease process including MS, ALS, and Alzheimer's disease. In addition, phospholipid methylation may be involved in modulation of NMDA (glutamate) receptors, acting to control excitotoxin damage.

Methylation as one piece of a more complex puzzle

In general, single mutations or *biomarkers* are generally perceived as indicators for specific health issues. However, it is possible that for a number of health conditions, it may be necessary to look at the entire methylation pathway as a biomarker for underlying genetic susceptibility for nonideal health. It may require expanding the view of a biomarker beyond the restriction of a mutation in a single gene to a mutation somewhere in an entire pathway of interconnected function.

This does not mean that every individual with mutations in this pathway will have one of the health conditions listed above. It may be a necessary but not a sufficient condition. Most health conditions in society today are multifactorial in nature. There are genetic components, infectious components and environmental components. A certain threshold or body burden needs to be met for each of these factors in order for multifactorial disease to occur. However, part of what makes the methylation cycle so unique and so critical for our health is that mutations in this pathway have the capability to impair all three of these factors. This would suggest that if an individual has enough mutations or weaknesses in this pathway, it may be sufficient to cause multifactorial health issues. Methylation cycle mutations can lead to chronic infectious diseases, increased environmental toxin burdens and have secondary effects on genetic expression.

Before we get to 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 SNP variation, it does not mean that the activity of the gene is completely “off”. It may simply mean it functions at a 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.

Just as the physical location of your hometown will not change, your genetics will not change over time either. For this reason these test results will serve as a road map for your future. Knowledge of your genetics is like having an ultrasound that allows you to see inside 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.

Nutrigenomic test results should help to put your mind at ease by giving you suggestions that you can act on. Nutrigenomics is a form of genetic testing that supplies information that can translate into positive constructive action. Dr. Yasko sees the ultimate goal of nutrigenomic testing to serve as a guide toward proper supplementation to bypass genetic weaknesses identified by SNP results.

Get started with these six simple steps

1) Get Your Glutamate and Gaba levels in balance and lay the groundwork for basic support

Excess glutamate relative to gaba can over excite your nerves. Glutamate works with calcium to stimulate your nervous system. Some stimulation is a good thing, but too much stimulation can leave you feeling nervous, twitchy and unable to sleep. The goal is to keep glutamate in balance so that you gain the benefits from it without having so much that your system is unbalanced:

- Be Calm Spray contains a number of ingredients to help balance excess glutamate. One of those ingredients is low level lithium support. This is a particularly important mineral, not only in terms of helping to control glutamate but lithium also helps with B12 transport. You want to be sure lithium is in balance before adding B12 so that you do not run the risk of further depleting potentially already low lithium levels.

- Resveratrol Glutamate balancing spray which is a special form of resveratrol can be another help for keeping glutamate in check as well as helping with pain or discomfort in the body.

- 1 to 3 capsules of the general vitamin can help with overall nutritional support. This is a uniquely formulated general vitamin with specific forms of vitamins and minerals to optimize health. The general vitamin is iron free as iron drives bacterial virulence. It is also copper free to help to achieve an optimal zinc/copper ration. It also contains highly specific forms of B vitamins that take into account nutrigenomic issues and low doses of a range of minerals that Dr. Amy has identified to be lacking in many individuals with methylation cycle SNPs.

- CoQ10 Spray to help with energy and for your muscles. CoQ10 is especially important for anyone taking cholesterol lowering medication but is something all of us can benefit from.

- SDE (special digestive enzymes) to help your body process food and to keep your pancreas well supported for balanced blood sugar. One SDE can be taken with dinner or with larger meals during the day. Not all digestive enzymes are created equal, and

SDE are special in that they have extra support for pancreatin in addition to other enzyme support.

- 1 to 2 sprays of Amino Assist spray. We all know we need protein, and the building blocks of protein are amino acids. Rather than eating a protein bar to get your amino acids, this special blend helps to give your body some of the key amino acids that it needs for daily function. For additional support you could also add in 1 or 2 Amino Assist capsules.

- 1 Ultimate B Complex. Your body needs B vitamins daily as they are water soluble and so they don't stay in your system. There are a number of different forms of each of the B vitamins and Ultimate B contains special forms of B vitamins along with a source of low dose PQQ the newest member of the B vitamin family.

With only three types of capsules and four sprays you can start today on your Road Map to health.

2) Get Short Cut Support in place to get the cycle moving

Although the ultimate goal is to get the long route around the cycle working, this can cause excretion of toxins from the body. While detoxification is a good thing, it can also allow for symptoms during the detoxification process. For that reason, getting the cycle moving by supporting the short cut helps to restore methylation function while limiting detox reactions. Once the short cut is working, and lithium is in balance then B12 can be gradually increased and finally MethylMate A + B (or equivalent source of 5 methyl THF, low dose folinic, nucleotides, lactoferrin, biopterin, phospholipids). *While there are soy free options for PS/PC Dr. Amy prefers the use of PS/PE/PC with PI whenever possible rather than just using a soyfree PS + PC.*

For short cut support consider:

PS/PE/PC gel cap + SAMe (IF tolerated)
Soy free PS if a non soy form of PS is required along with a separate source of PC
Vita Organ as a secondary source of PS as well as to help with nutrient absorption and gut pH
Daily DHA + few drops methylation RNA

3) Assess and support lithium levels

Lithium not only plays a role in mood, glutamate control and limiting aggression, but also has been shown to be involved in B12 transport. Many adults as well as individuals who are MTR A2756C + tend to have lower levels of lithium as judged by hair metal analysis (HMT). Supporting with higher levels of B12 before having ascertained that lithium is in balance may lead to further depletion of lithium levels. For this reason Dr. Yasko highly suggests running a hair metal test (HMT), and/or blood lithium test along with a urine essential element test (UEE)

to assess the lithium level in the system. If lithium levels are low in hair and blood or urine, or if very high level lithium excretion (in the absence of support is seen in urine) consider additional lithium supplementation with your doctor before moving on to B12 support. Sources of lithium support can include Be Calm Spray, Lithia water, low dose lithium orotate, and the new upcoming general vitamin called "*All in One"*. The level of support needed should be determined by a combination of running biochemical tests (UEE, HMT, blood lithium) as well as consultation with your health care provider.

4) Determine Your Ideal Form of B12

Once your lithium levels are in balance and short cut support is in place it is time to start to increase B12 support and to customize your supplement plan to optimize your health, based on your personal results. Just as the GPS system in your car guides you in unknown areas when you are driving, so too can your nutrigenomic results guide you in individualizing your personal healthcare. Not all of us can tolerate caffeine. We all know people who can drink espresso just before bed and fall asleep like a baby and others who are shaking from a single cup of dilute coffee. These differences in part reflect individual tolerances to certain compounds in coffee. These effects are similar to the response people can have to different forms of B12. We need B12, it is a critical B vitamin and by now all of you are getting some low dose B12 support from the General Vitamin and Ultimate B complex. The forms of B12 in those vitamins are designed to be tolerated by all, but now it is time to add some specific B12 based on your nutrigenomic results. The chart below will help you to determine which form of B12 might be best tolerated by your system. There is a more detailed description of the types of B12 along with references for their use after the chart if you want more information than simply knowing which type of B12 might be best suited based on your nutrigenomics.

COMT V158M	VDR Taq	B12 types that should be tolerated
- -	++ (TT)	All three types of B12
--	+- (Tt)	All three types with less methyl B12
--	-- (tt)	Hydroxy B12 and Adenosyl B12
+-	++	All three types with less methyl B12
+-	+-	Hydroxy B12 and Adenosyl B12
+-	--	Hydroxy B12 and Adenosyl B12
++	++	Hydroxy B12 and Adenosyl B12
++	+-	Hydroxy B12 and Adenosyl B12
++	--	Mostly Hydroxy B12

While this chart helps to guide you on the choice of the type of B12 based on nutrigenomics, it is also important to pay attention to what your body is telling you. In spite of nutrigenomics if you are having trouble tolerating methylB12 then listen to your body and use hydroxyl with some adenosyl B12 instead. This is particularly true for adults who often have a more difficult time with any supplements that can trigger detox including any methylB12 support.

Why it is so important to have a form of B12 that you can tolerate

Vitamin B12 is a water soluble vitamin. This means that it doesn't stay in the body for a long period of time and that more frequent support with B12 may be needed to maintain healthy B12 levels in the body.

- Vitamin B12 is important for energy, for balance related sports, for endurance sports, for healthy red blood cells, for memory, among other roles in the body.

- Vitamin B12 can be depleted by drinking alcoholic beverages, a poor diet, certain medications and as we age.

- Lack of B12 has been associated with fatigue, alcoholic liver disease, anemia, cancer, ulcers, dementia, neural tube defects, depression and memory loss.

- Higher levels of B12 correlate with improved balance, energy and endurance in athletics.

Different types of B12 work best for different people

Vitamin B12 also called cobalamin can include hydroxyl B12, methylB12, cyanoB12 and adenosylB12. Many vitamins, including B12, are not active in the form in which they are normally found in food, instead the body needs to convert the B12 into a form that it can use directly. B12 is needed for the proper functioning of a number of different enzymes in the body, however not all types of B12 are equal and not all types of B12 can be easily changed to what is needed for critical reactions in the body. Hydroxy, methyl and adenosyl are all forms of B12 that are used directly by reactions in the body. CyanoB12 must be converted for use in the body and as the name suggests, cyanocobalamin contains a cyanide molecule.

- **MethylB12** can be used in the body, though it cannot be tolerated by everyone. Those who get jittery from caffeine, coke, tea may not react as well to methylB12. Many adults don't do as well with methyl B12 in spite of their nutrigenomics and so it is fine to choice an alternative form.

- **AdenosylB12** is a special form of B12 that is important in the energy cycle in the cells of your body. It is important to have adenosyl B12 but it is not as versatile as other forms of B12 so it can be used in lower doses.

- **Hydroxycobalamin**, or hydroxyB12 is a unique form of vitamin B12, which is more easily converted to the form that is actually used for reactions in the body. This might cause you to ask, why doesn't everyone use high dose hydroxylB12 in their formulations? Well, Hydroxycobalamin (Hydroxy B12) is more difficult to work with, harder to keep in an active form and more expensive than some other forms of B12, such as cyanoB12. For this reason, many other products do not contain hydroxyl B12 and instead use cyanoB12.

- **CyanoB12** contains a cyanide molecule. So when you take cyanoB12 your body must first turn it into hydroxyB12 in order to use it, and then must find a way to get rid of the toxic cyanide molecule. We all know cyanide is a poison even if the rest of the B12 molecule is good for you. The body actually uses hydroxyB12 in order to detoxify cyanide. So, not only is cyanoB12 not the form your body ultimately needs, but taking higher doses of cyanoB12 may actually deplete your hydroxy B12. So why would anyone use cyano B12 if it can be toxic? Well, in low doses it may be helpful for the eyes, but for the most part cyanoB12 is used because it is much less expensive, and a form of B12 that is easier to keep in a stable.

Options for additional B12 support:

- Hydroxy Mega Drops
- Get B12 Spray
- Black Bear Spray
- Black Bear Drink
- Adenosyl Mega drops
- Methyl Mega drops
- B12 injections (if possible hydroxyB12)
- Dibencozide (adensyl B12) tablets
- Activated B12 Guard
- Low dose more limited support with cyanoB12 (as long as hydroxyl support is also in place)
    - B12 gum
    - B12 patch

For a complete list of B12 support:
http://www.holisticheal.com/complete-b12-list.html

5) The remainder of long route support

In addition to B12 support the long route around the cycle also uses folate. Those with MTHFR mutations cannot use plain folate ideally, and instead the use of 5 methyl THF helps to bypass MTHFR mutations. MethylMate B is a liquid form of 5 methyl THF that allows you to adjust the dose of 5 methyl THF down to very low levels. This is important as the addition of 5 methylTHF will often be the piece that triggers significant detox of toxic substances from the body. Having the ability to adjust this process with exquisite control is a real plus as it allows you to adjust the dose of 5 methylTHF and hence to have some control over the rate of detox. Starting with one drop or even one dilute drop is possible and then gradually increasing to 3 drops daily if tolerated. Dr. Amy is well aware that there are other programs that use much higher doses of 5 methyl THF. While this is not her preference at all, you can increase the amount of MethylMate B as needed to adapt to whatever program you are using

MethylMate A contains the ingredients to help to support the remainder of the methylation cycle. It includes nucleotides to take the pressure off the cycle and the immune system for generating nucleotide building blocks. It includes a low dose source of folinic acid as well as lactoferrin to support proper balance for the SHMT portion of the cycle (although those who are SHMT + should consider additional SHMT support). MethylMate A also includes low dose support for natural biopterin,as well as additional short cut support for PS, PE, PC, PI. One or more MethylMate A is sufficient for support of the cycle

6) Customized support Beyond B12

Now that you have determined the ideal form of B12 based on your personalized nutrigenomic profile it is time to look at adding in support to help bypass other imbalances that have been detected. Remember the mutations we are looking at are in a nutritional pathway. The beauty of this is that we can look at these well known pathways and see where supplements can be added to bypass imbalances that may show up on your test. Look at your test results and find any that are listed as ++ or +-. Then refer to the table below to look at suggested supplementation that can be considered to help bypass these issues.

NOTE:
The ++ designation means that both copies of the gene are affected while + - means that only one of the two copies in the body has this mutation. In general those who are ++ may want to use slightly higher doses of supplements than those who are + -.

Gene Name	+ + or + -
COMT V158M	MethylMate A caps and MethylMate B drops and B12
COMT H62H	MethylMate A caps and MethylMate B drops and B12
COMT P199P	MethylMate A caps and MethylMate B drops and B12
VDR Taq (TT)	Vitamin D spray
VDR Fok	Fok Pancreatic caps
MAO A R297R	Seromood
ACAT 1-02	ACAT/BHMT caps with each meal
MTHFR C677T	B12 and MethylMate A caps and MethylMate B drops
MTHFR P39P	B12 and MethylMate A caps and MethylMate B drops
MTHFR A1298C	MTHFR A1298C caps
MTR A2756C	MethylMate A caps and MethylMate B drops and Lithium support and low dose B12 and Be Calm spray and low dose MTR/MTRR/SUOX caps
MTRR A66G	B12 and MethylMate A caps and MethylMate B drops
MTRR H595Y	MethylMate A caps and MethylMate B drops and Lithium support and B12
MTRR K350A	MethylMate A caps and MethylMate B drops and Lithium support and B12
MTRR R415T	MethylMate A caps and MethylMate B drops and Lithium support and B12
MTRR S257T	MethylMate A caps and MethylMate B drops and Lithium support and B12
MTRR A664A	Amino Assist Spray/Caps and VitaOrgan
BHMT 1	VitaOrgan and ACAT/BHMT caps with meals
BHMT 2	VitaOrgan and ACAT/BHMT caps with meals
BHMT 4	VitaOrgan and ACAT/BHMT caps with meals
BHMT 8	VitaOrgan and ACAT/BHMT caps with meals
AHCY 1	AHCY/SHMT caps with meals
AHCY 2	AHCY/SHMT caps with meals
AHCY 19	AHCY/SHMT caps with meals
* CBS C669T	Black Bear Spray and low dose MTR/MTRR/SUOX caps and * CBS RNA
* CBS A360 A	Black Bear Spray and low dose MTR/MTRR/SUOX caps and * CBS RNA
* CBS 212	Black Bear Spray and low dose MTR/MTRR/SUOX caps and * CBS RNA
SUOX S370S	Black Bear Spray and low dose MTR/MTRR/SUOX cap
SHMT C1420T	SHMT spray and caps
NOS D298E	MTHFR A1298C capsules

* CBS issues

Those who are CBS + may tend toward excessively high taurine levels on a urine amino acid (UAA) test once methylation support is in place. Until adequate support for the methylation cycle is in place the impact of the CBS SNP is often not seen. As I have described before you can think of the CBS SNPs as a leaky plug in a bath tub. Until you fill the tub with water you cannot tell that the drain plug isn't sealing properly and is causing the tub water to flow down the drain instead of filling the tub. In a similar fashion, you cannot see the impact of the CBS SNP until you have sufficient methylation support in place such that the cycle is filling and at that point the taurine levels will rise well above the 50th percentile on a UAA if more CBS support is needed. Work with your doctor to use follow up UAA testing to monitor taurine levels and use the CBS RNA ONLY as needed to keep taurine in balance as determined by regular UAA testing for taurine levels and in conjunction with your doctor.

Special Considerations

We all encounter instances when we need some additional nutritional support, whether it is due to stress, heartburn, a head cold, too much social partying or simply a time period when we are feeling drained of energy. In addition to the general support, B12 support and specific nutrigenomic support listed above, during certain circumstances using some extra supplementation can make a big difference in recovery time.

Head Colds
Naturomycin Spray
Naturomycin Caps
Immune Boost Spray
Zinc Lozenges
Seasonal Support caps

Sleep Issues
Sleep Spray

Social Partying
A1298C/Liver Support Caps
GSH
Black Bear Spray and Drink

Energy/Fatigue
Extra B12
Black Bear Spray and Drink

Antioxidant support
Ultifend
A1298C caps
Reservatrol Glutamate/gaba spray

Heartburn
Peptimycin

Limited Sunshine
Vitamin D spray

Additional Protein Support
Amino Assist Caps
Amino Assist Spray
VitaOrgan

Metal Detox
Metal Away
Detox Away

Different Methodologies for Nutrigenomic Testing

There are discrete reasons why Dr. Yasko chooses to use blood spot samples and the MassArray technology to screen for these SNPs rather than using saliva samples and BeadChip technology.

This is not to minimize the value of the BeadChip technology. It is a wonderful tool for what it was designed for, to screen a large number of genes in a rapid time frame. This is great if you are looking for a broad picture and not certain which SNPs in particular you are most concerned with. However, given the fact that we know the SNPs we are interested in looking at critically, from Dr. Amy's vantage point it makes more sense to use a technique designed to do just that. In fact, in a number of research situations the BeadChip technology is initially used to narrow down which SNPs are of interest and then use the MassArray technique to more critically study those SNPs of interest (Mol Ecol.Suppl 1:132-46 2010 Mar;19 and Genet 2008 4(4)).

The bottom line is to pick the right tool to do the job that you are looking to accomplish. "*Different technologies are appropriate for different types of projects and scales of SNPs to be genotyped"* (http://cshprotocols.cshlp.org/content/2009/11/pdb.top62/F1.expansion.html).

There are several major differences between the test Dr. Yasko prefers and other tests that are available. One point of difference is in terms of the technology used to analyze the samples and another is the sample quality itself. Dr. Amy is more comfortable with the results obtained using the Mass Array TaqMan technology. According to the literature, MassArray technology is greater than 99% reliable and in some cases has been reported to be 100% accurate in looking at SNPs. *"Given sufficient DNA concentration and quality, the designed iPLEX/TaqMan test had an accuracy of 100% for the designed assays. These results suggest that the combined iPLEX/TaqMan test is an outstanding tool for identification of recurrent mutations"* (Combined iPLEX and TaqMan Assays to Screen for 45 Common Mutations in Lynch Syndrome and FAP Patients J Mol Diagn. 2010 January; 12(1): 82–90).

BeadChip technology, is a faster, less expensive method that can look at a larger number of SNPs at one time, but with a potentially lower sensitivity depending on the way in which sample bias is corrected for. *"In the interests of practicalities and cost, these results suggest that single samples can generate reliable data, but only after careful compensation for technical bias in the experiment. We recommend that investigators appreciate the propensity for such variation… and that the use of suitable correction methods become routine during the statistical analysis of the data."* (Correcting for intra-experiment variation in Illumina BeadChip data is necessary to generate robust gene-expression profiles. BMC Genomics 2010 11:134.) Thus, while the level of sensitivity may be as high as 94%, for any given sample on any given SNP for any given individual it may also be as low as 75%.

To put this in less technical terms, go back to the concept of thinking of SNPs like accidents on a highway. These accidents on the highway of the methylation cycle cause issues in the traffic flow along those highways, necessitating that you take a detour to get around the traffic accident. So, working with that analogy think of BeadChip as a traffic helicopter that flies high up above the highway to look to see where there may be issues on the road. This helicopter is responsible for a very large area (ie the entire state of Maine) and so it is flying quickly to cover a large region. It is able to detect areas where traffic is stopped but may not be able to discern between a minor fender bender, a serious fatal accident or a car stopped by the side of the road to ask for

directions or one whose radiator has overheated. In order to get more specific details of what has caused the traffic delay the helicopter can call in local police to have actual ‘feet on the ground’ to assess the situation more closely. Compare this to MassArray, where we know the actual locations we are interested in. We know the exact intersection/cross streets where we want to know if there is a traffic issue or not. So ahead of time we have 'eyes on the ground’ placed at those precise 30 intersections looking to see if there is an issue or not. Clearly both techniques have value but in our situation, where we know which SNPs we are most interested in the greater accuracy and sensitivity of having eyes on our 30 specific intersections ahead of time makes the most sense for the Yasko protocol.

The second area of difference between BeadChip and MassArray options is the sample type itself. The BeadChip is using saliva and the MassArray test for the methylation SNPs (or blood draws from your doctor and sent to a test lab that does SNP testing) use blood samples. Initially we used saliva samples for testing. Dr. Yasko became concerned that saliva could give false positive/negative results in spite of the sophisticated Mass Array technology that was being utilized to identify SNPs within the samples. There are internal checks and balances in the SNP panel and we were finding that many of the saliva samples had to be rerun multiple times or even new samples submitted to reduce questionable results. The samples were rerun until it was felt that all SNPs were evaluated accurately but this caused time delays and in some cases multiple sample collections and reruns. The lab was able to design a simple blood spot method to have the ability to limit the potential issues with some saliva samples while maintaining the convenience of in home testing. Studies by other researchers comparing the use of saliva versus blood for SNP testing have found that saliva yields results 89% versus blood at 99% results (Hu Y, Ehli EA, Nelson K, Bohlen K, Lynch C, et al. (2012) Genotyping Performance between Saliva and Blood-Derived Genomic DNAs on the DMET Array: A Comparison. PLoS ONE 7(3): e33968. doi:10.1371/journal.pone.0033968). To expand upon the traffic helicopter analogy, using saliva samples may be creating fog so that it is more difficult for that helicopter to see what is going on. Thus the combination of the lack of eyes on the ground at specific intersections and the potential for fog may make that technology less applicable to a nutrigenomic situation where we know exactly which specific intersections we are interested in.

The third area of difference is in what the test is trying to accomplish. As alluded to above, the BeadChip technology is designed to give you an overview of a large number of genes that may or may not be in the same pathway. The Mass Array SNP test is looking at specific, well defined genes in a very particular pathway. So, 30 very specific genes in a pathway that is critical for health as opposed to a much larger and broader overview. To expand upon the difference between this test and others is to think of it in terms of a road map. If you wanted to travel from your hometown to Bethel, 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 to get from your hometown to Bethel, Maine 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 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 a map, but without any of the specific information between those two points. Without the details, you do not know if the route you may choose has been closed, if the bridge is out, of if there is a detour that will add more time to your travel. Given only a starting and stopping point, or even if you are just missing ***a few key points*** on the map means the rest of the trip may simply be guesswork. The nutrigenomic test that Dr. Yasko prefers is designed to take the guesswork out of your trip to health and wellness. Compared to other tests that look at isolated genes in a wide range of pathways, focusing on the methylation cycle allows you to look comprehensively at a very critical pathway in the body and from that construct a personal road map to health and wellness.

There is one final **critical point** that needs to be reiterated with respect to SNP testing. There are approximately 25,000 genes in the human genome. Dr. Yasko personally believes in only looking at SNPs that are in well defined pathways where it is clear how to add nutritional support to bypass imbalances. Having a laundry list of SNPs without a way to use nutritional support is not consistent with the way she approaches health. So, whether you have a test that gives you 1000 or 5000 SNPs this is still only a fraction of the total number of genes in your body and frankly having more SNPs is not the issue. The real question is whether the SNPs you have are in a pathway that has been characterized so you know what to do to help restore your body to health. The reason Dr. Yasko focuses on the methylation cycle is that it is a well defined pathway, it is very clear where nutritional support can bypass mutations and the pathway we look at IS the system the body uses to edit and correct problems with other genes. So regardless of how many other SNPs there are in the 25,000 or so other genes in the body, IF those genes are regulated by methylation, then having your methylation cycle in balance gives you the tools you need to help to turn on or off those other genes that are NOT part of the 30 SNP methylation panel. This is called ***epigenetics***, and Dr. Yasko has given entire talks just on this topic. Having the methylation cycle function optimally and bypassing SNPs in this pathway allows the global editing function in your body to help to correct issues with any number of other genes in the system. THIS is why this pathway is so critical for health and wellness.

REMEMBER your DNA does not change. This is a test that you will run ONCE in your lifetime. Unlike the follow up biochemical testing that you run routinely to check that the supplementation you are using is actually making a difference, a nutrigenomic test focusing on the methylation cycle is something you will run only one time. You will work with your doctor to determine supplementation based on these SNPs for the rest of your life.

If you have already run a potentially less sensitive test, that is okay. The SIMPLIFIED road map should still help you to get a sense of supplement choices to help you to bypass SNPs that were identified by any test.

Additional Scientific Background and further testing

As already explained your DNA will not change so once you have nutrigenomic test results those will not change over your lifetime.

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 or hair.

Biochemical testing can be used to assess the effect of supplementation on your system. Ideally, the goal is to use the knowledge of your genetics to make informed decisions on how to supplement and bypass weaknesses in your system. Then to use regular biochemical testing to monitor the progress of your supplementation to bypass mutations.

You can go to:
http://www.holisticheal.com for more information on biochemical testing.
http://www.holisticheal.com/complete-list-of-health-tests.html

For those of you who are interested in more in depth information about the Methylation Cycle such as an understanding of which genes have increased activity, which have regulation problems and those which have reduced activity you can find more advanced information in the book, Genetic Bypass by Dr. Yasko or by joining the discussion group at http://www.ch3nutrigenomics.com.