VITAONE®

VitaOne® Complete Methylation Genetic Test

Precision Insight into Your Body's Core Methylation Genes

Patient ID: M-0001
Patient Name: Sample report

"Within our DNA lies the blueprint of our past and the potential of our future."

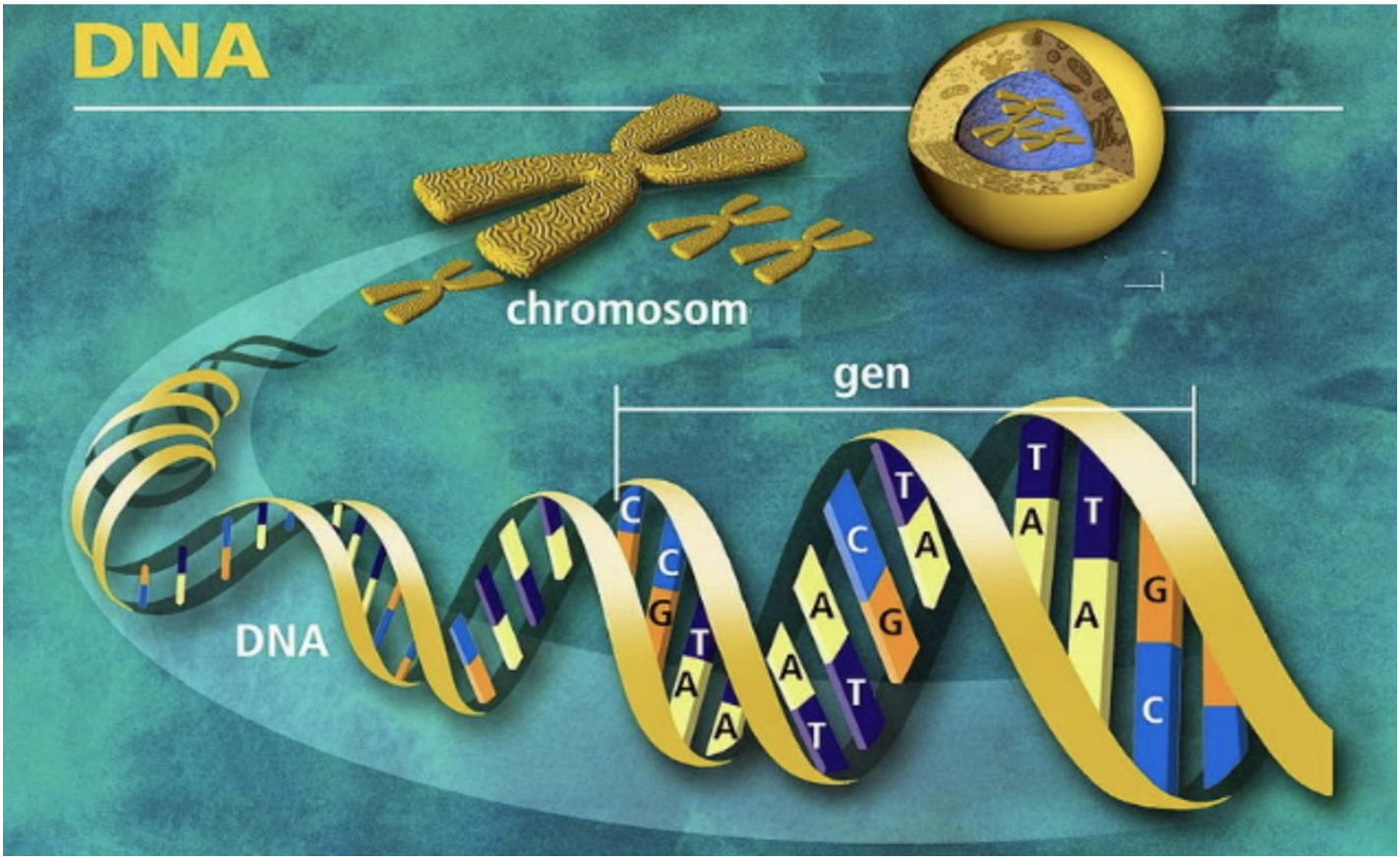
"The beauty is that even a slight genetic variation could have a greater impact on your health and longevity."

"Decode your DNA, Redefine your destiny"

Introduction

At VitaOne, we believe your DNA is not your destiny — it is your blueprint.
Through advanced genomic analysis and evidence-based interpretation, we help you understand how your genes influence detoxification, methylation, hormone balance, metabolism, and longevity.

Our precision insights empower you to take targeted action through nutrition, lifestyle, and supplementation — unlocking your optimal health potential.



VitaOne – The Blueprint of Your Health & Longevity

We humans as individuals are so unique from our fingerprints, facial structure to intelligence and self-confidence because of small variations in our genetic code called as Single Nucleotide Polymorphisms (SNPs). SNPs occur normally throughout a person's DNA. The human genome contains a vast number of SNPs, with estimates ranging from 4 to 5 million in a typical individual. Most SNPs have no effects on human health or development. But there are a significant number of SNPs that can have a bigger impact on health and influence everything from disease risk to response to medications.

VitaOne Genomic Insights analysis over such 330 clinically relevant significant genetic variations or SNPs and provides tremendous opportunities for personalized prevention & treatment plans. You can visually see, and learn, how your unique genetic pathways function. Getting your SNPs tested unlocks a wealth of insights into optimizing wellness and avoiding chronic illnesses you may be genetically predisposed to. The prospects of unlocking your genetic blueprint to guide tailored lifestyle and wellness recommendations is compelling. Personalized Solutions based on genetic testing is "the Future of Healthcare".

Genes cannot be switched on and off by themselves. Factors such as our environment, diet, lifestyle and relationships can influence our genetic expression through GXE interaction. Epigenetic mastery is the cornerstone of VitaOne Genomic Insights.

STEPWISE ACTIONABLE INSIGHTS

• Step 1 : Understand how the Epigenetic Control Points (Inhibitors & Inducers) influence genetic expression.

• Step 2 : Ensure repletion of Co-factors for optimal enzyme activity.

• Step 3 : Know how your Genetic Polymorphisms (SNPs) are impacting enzyme activity (Slow/ Fast) or receptor function (upregulated/ downregulated).

• Step 4 : Precision diet / Supplementation and Lifestyle modification to negate the ill effects of genetic variations.

Although we decode your whole DNA to understand the susceptibility to diseases, we simply don't stop with that process. Perhaps we provide the most epigenetic influences that control the epigenetic expression of each genetic variation without changing the genetic code thereby providing a tool to empower you.

Even if you are having genetic variations, just relax !! You can very well lead a healthy life with our epigenetic tools.

Representations

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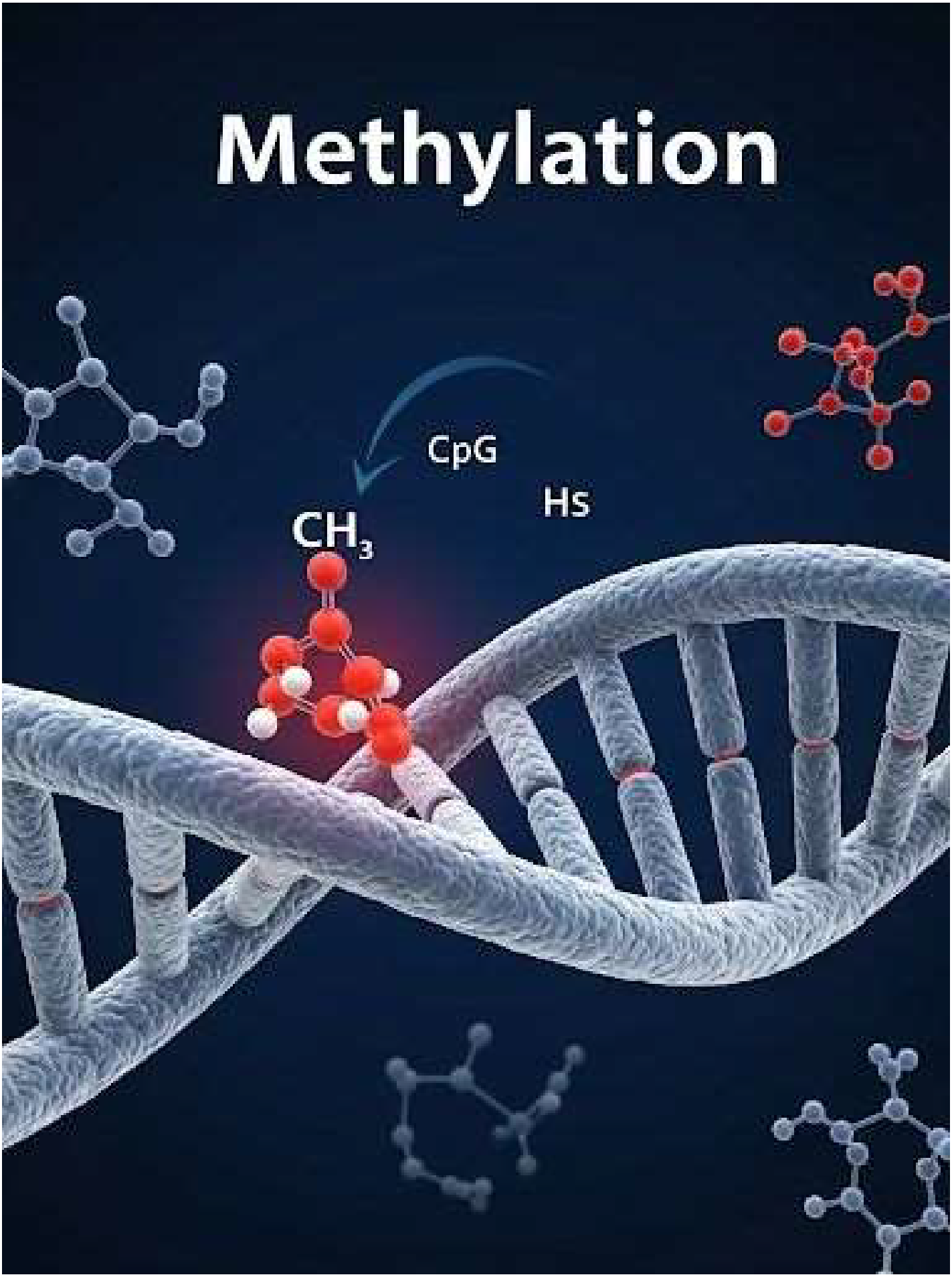
Methylation



Methylation is a biochemical process in which methyl groups (CH3) are transferred or donated between molecules, thereby changing their structure and function. This happens billions of times per second in every cell throughout the body. The methylation cycle is dependent on amino acids, vitamin cofactors, and minerals obtained from the diet to ensure adequate function of this biochemical pathway.

Methylation pathways are vital for regulating gene expression, cellular processes, and detoxification. They involve the addition of a methyl group (CH3) to DNA, proteins, and other molecules, which affects their function and activity. Key aspects of methylation include:

1. DNA Methylation: The addition of methyl groups to DNA can turn genes on or off, playing a role in gene expression and cellular differentiation. Abnormal methylation patterns are linked to diseases like cancer and neurological disorders.

2. Folate Cycle: Folate (vitamin B9) is essential for the methylation process, especially in the conversion of homocysteine to methionine. Methionine is a precursor for S-adenosylmethionine (SAMe), a key methyl donor.

3. Homocysteine Regulation: Proper methylation helps regulate homocysteine levels; a type of amino acid linked to heart disease when elevated. Deficiencies in B vitamins (B6, B12, and folate) can impair methylation and lead to high homocysteine levels.

4. Gene-Specific Methylation: Methylation is also involved in regulating important genes like tumor suppressors and immune system genes, influencing cancer risk, autoimmune disorders, and inflammation.

Methylation is crucial for cell function, genetic stability, and detoxification. Disruptions in methylation pathways can contribute to genetic diseases, cardiovascular problems, and neurological conditions like Alzheimer’s.

Methyl groups are switches that turn on and off genes based on environmental cues. This is called Epigenetics. Additionally, methyl groups signal which hormones, brain chemicals, and amino acids need to be broken down and removed, maintaining a healthy balance in the body. The “methylation cycle” involves an interplay between folate metabolism, methionine metabolism, and homocysteine transsulfuration. Rate limiting enzyme is MTHFR. The body continually adapts these interconnected pathways in order to maintain homeostasis.

There is a relative balance that exists between the methylation and transsulfuration pathways. This balance ensures that adequate levels of glutathione are produced to counteract oxidative stress and that an adequate amount of SAM is made for methylation reactions. However, key amino acid deficiencies, a lack of vitamin and mineral cofactors, genetic enzymatic predispositions, and a wide array of oxidative stressors can impact multiple enzymes leading to a disruption in a patient’s overall methylation status.

Methylation is essential for

• Creatine Production for Skeletal Muscle Contraction

• DNA and RNA Synthesis

• Gene Regulation (Epigenetics)

• Hormone Regulation and Detoxification

• Energy Production

• Cell Membrane Repair

• Fat Metabolism

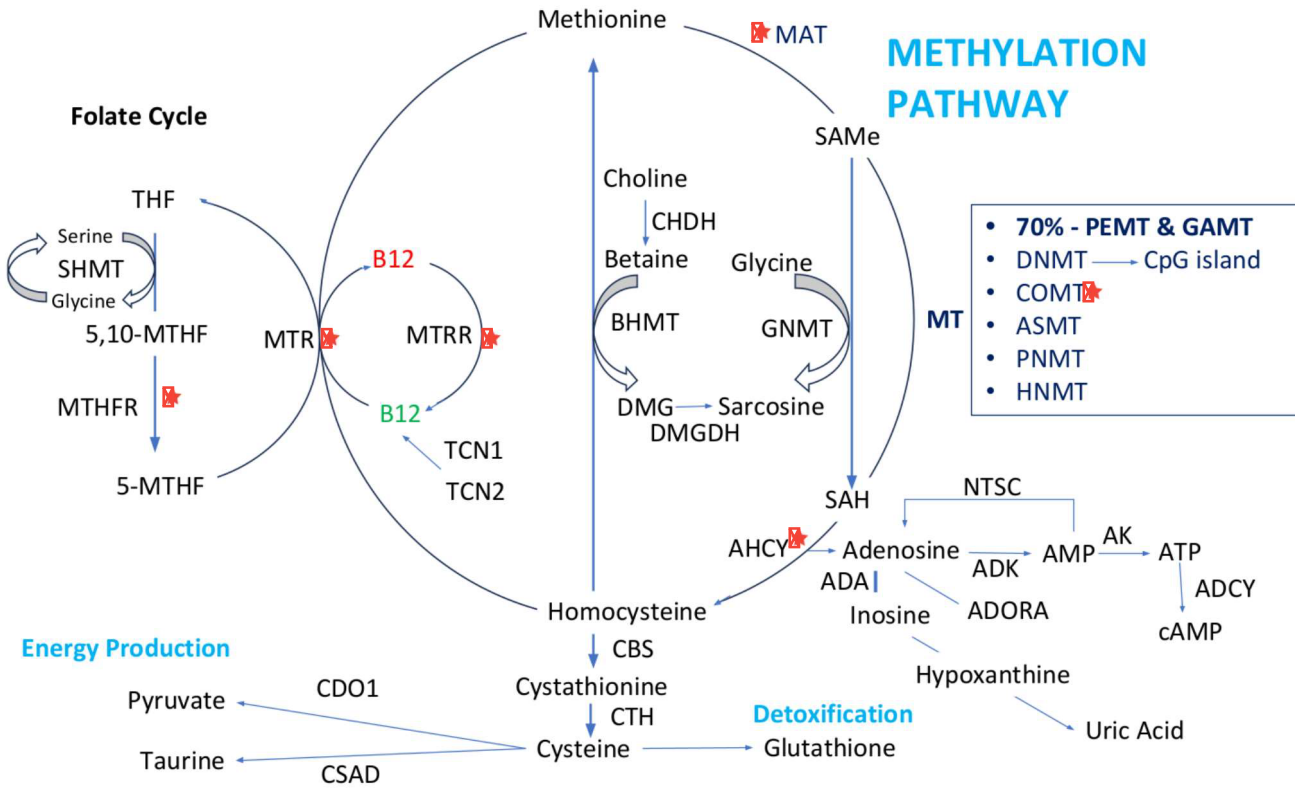
• Myelination

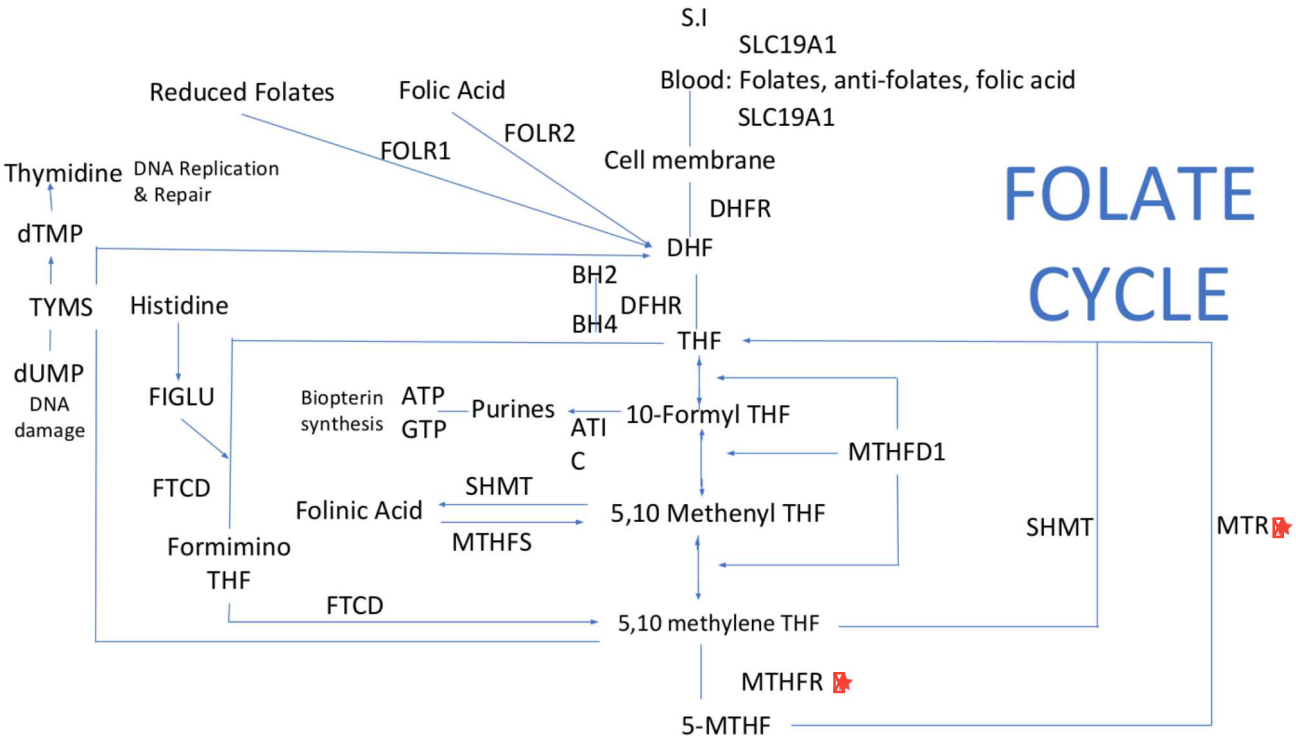
• Immune Function

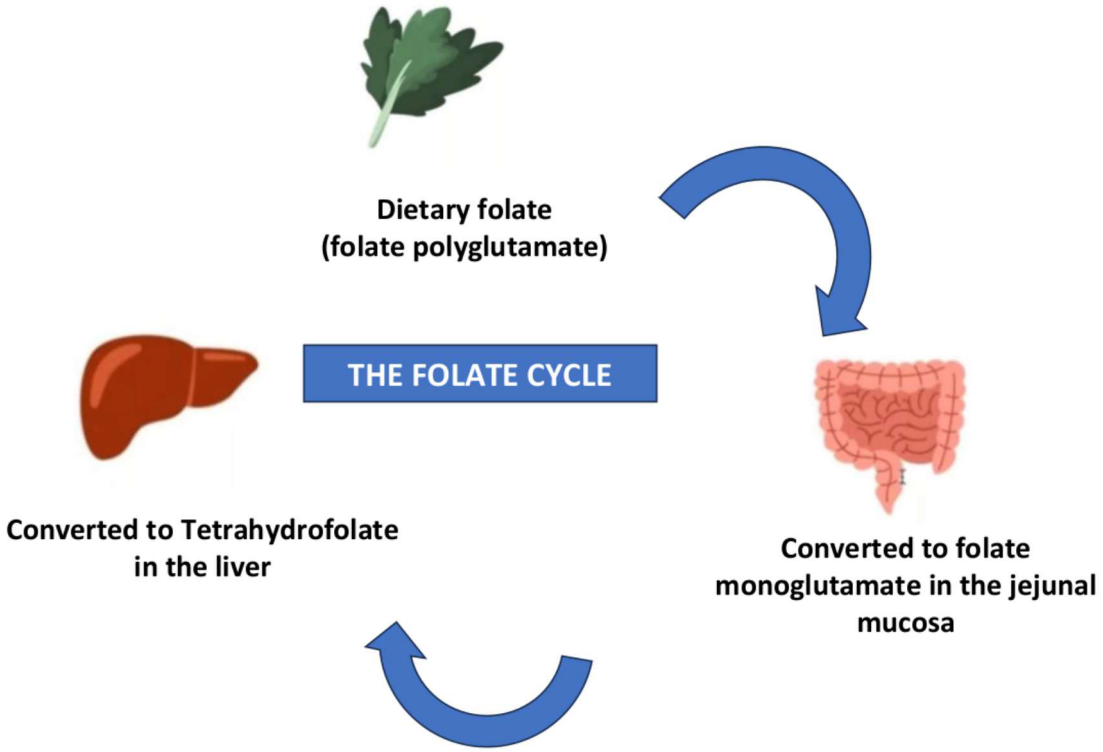
• Neurotransmitter Production and its Metabolism

• Vascular Endothelial Function and Nitric Oxide Production

GENE	SNP	Genotype
AHCY	rs819147	TT
AHCY	rs13043752	TT
COMT	rs4680	GA
COMT	rs4818	CG
COMT	rs4633	CT
COMT	rs6269	GG
MAT1A	rs3851059	GA
MAT1A	rs7087728	GG
MTR	rs1805087	AG
MTR	rs3768142	GG
MTRR	rs1801394	AG
MTRR	rs1532268	CT
MTHFR	rs1801131	TG
MTHFR	rs1801133	GG







AHCY

ACHY makes SAHH (S-Adenosyl Homocysteine Hydrolase) is a bidirectional enzyme which converts S-Adenosyl Homocysteine to Adenosine & Homocysteine. This step not only sustains the flux of methionine sulfur towards cysteine but also plays a critical role in the role of biologic methylations. Elevated SAH levels can interfere with methylation processes and detoxification.

Cofactor: B3

Epigenetic Control Points

Inhibitors

Heavy metals, Copper

Mercury

Oxidative stress

Inducers

TMG

SAMe

Fasting

SNP: rs819147

Genotype: TT

Reduced enzyme activity can contribute to higher levels of homocysteine and can
disrupt the body's methylation balance, hypermethioninemia.

SNP: rs13043752

Genotype: TT

Reduced Enzymatic activity

Interpretation & Actionable Insights

SAH is hydrolyzed to homocysteine; however, this reaction is readily reversible, and the dynamics strongly favor SAH synthesis. Therefore, any elevation in homocysteine will lead to an increase in SAH. In spite of the reversible nature of this reaction, efficient cellular removal of homocysteine allows sustained SAH metabolism and homocysteine production. SAH accumulation is implicated in many chronic clinical conditions. SAH is a potent feedback inhibitor in methyltransferase reactions. SAH's pathogenicity lies in its binding affinity for, and inhibition of, methyltransferase enzymes within many tissue components, including DNA, RNA, phospholipids, and others. (vascular cell phenotypic changes and atherosclerotic disease development). Plasma SAH level is a more sensitive marker for clinical cardiovascular disease, renal disease, and Alzheimer's disease than plasma homocysteine. Methylation reactions are ultimately dependent on SAH removal. Genetic SNPs, or nutritional deficiencies that hinder Hcy or adenosine metabolism, can induce SAH accumulation and subsequent hypomethylation defects, which are implicated in a variety of diseases. Nutritional therapies that encourage Hcy

Interpretation & Actionable Insights

metabolism (i.e. folate, B_{12}, betaine, choline) may passively lower SAH levels.

PMID: 10884384, 24004894, 21967576, 20413857

COMT

Catechol-O-Methyl Transferase is involved in Phase II detoxification and inactivates catecholamines & Catechol estrogens.
Genetic variations which decrease COMT activity leads to increased 4-OH Estrogens (damage DNA – Carcinogenic potential)
Slow COMT : More potential for Neurotoxic compound (in the presence of other ROS) "Dopamine Quinone"
If both COMT & MAO are functioning slowly more potential for neurotoxic 'Adrenochrome' formation.
HyperEstrogenism & Xenoestrogens increase COMT's workload.
COMT polymorphism has been implicated in risk of breast cancer, particularly in women with prolonged estrogen exposure; or in women with low folate and high homocysteine. It correlates with higher estrogen levels with estrogen replacement therapy.

Cofactors: Magnesium, SAMe

Epigenetic Control Points

Inhibitors

- Low Folates
- Low Vit D
- Increased Serotonin levels
- Increased Homocysteine levels
- Clutter & Disorganization
- Early life adversity
- Noisy Sleep Environment
- Avoid Stressful environment, Abuse, Assault, wi-fi, blue-tooth
- Excess Caffeine
- Excess Copper
- BPA
- Xenoestrogens

Inducers

- Infection
- SAMe
- Magnesium
- Vit C
- EGCG
- Omega-3

SNP: rs4680
Genotype: GA

Intermediate enzyme activity; balanced dopamine levels in the prefrontal cortex. Slightly increased risk for CAD.

SNP: rs4818
Genotype: CG

Slightly reduced risk of chronic postsurgical pain, fibromyalgia & TMJ disorders.

SNP: rs4633
Genotype: CT

Moderately increased COMT activity

SNP: rs6269
Genotype: GG

Fast enzymatic activity; lower dopamine levels & increased pain relief to morphine. Increased risk of Parkinsons disease related dementia (PDD)

Interpretation & Actionable Insights

rs4860 is often called the worrier or warrior variant. The G allele is linked to a higher COMT activity. People with GG are nicknamed the warriors as they breakdown stress-related chemical messengers more quickly which may help improve their performance under stress (thrive under stress). They are more likely to engage in combat sports. On the flip side, “warriors” may have lower cognitive performance under relaxed conditions. People with AA have lower COMT activity are nicknamed the worriers as they breakdown stress-related chemical messengers more slowly in the brain and are more vulnerable to stress. They become emotionally resilient with age. They have enhanced cognitive performance under relaxed conditions and a more pronounced placebo response due to higher dopamine levels.

PMID: 8807664, 12571159, 9407957, 30011860, 9702745 12359690, 18324659

MAT1A

Methionine Adenosyl Transferase 1A turns methionine to S-Adenosyl methionine (SAM-e)

MAT1A gene variant may be linked to DNA damage and other methylation issues (hypertension & stroke). MAT1A enzyme turns methionine to SAM-e. Supplementing with SAM-e may help reduce the impact of this variant. It is downregulated by oxidative stress, such as alcohol and free radical damage. MAT1A genotype modulates PUFA’s regulatory effect on Hcy metabolism. High dietary fat intake causes significantly high Hcy levels associated with increased risk of CVD & Stroke. Methylation activity impairment independent of Hcy levels, have an effect on cardiovascular risk!!!

Cofactors: Mg, K, ATP

Epigenetic Control Points

Inhibitors

LPS

IL-6, TNF-α

Hep B, Hep C

NO, CCL4

Alcohol

Mold

Inducers

Cofactors

Fasting

Low Methionine

SNP: rs3851059

Genotype: GA

Lower enzyme activity. The "A" allele is associated with higher homocysteine if their folate status is low. Intermediate risk of stroke. Infantile onset neurodegenerative disorder, Autism Spectrum Disorder, Facial Photoaging

SNP: rs7087728

Genotype: GG

Increased risk of stroke, hypertension, increased Oxidative DNA damage & decreased methylation capacity

Interpretation & Actionable Insights

Methionine adenosyltransferase (MAT) enzyme is highly conserved and regulated. The D18777A MAT1A SNP downregulates the enzyme's activity, decreasing SAM production. It showed that higher dietary fat intake is associated with significantly higher Hcy levels in patients with the D18777A SNP. This supports a hypothesis that the MAT1A genotype may modulate polyunsaturated fatty acids' regulatory effect on Hcy metabolism. This SNP showed significantly higher stroke rates. The findings suggest that methylation activity impairment, independent of Hcy levels, have an effect on cardiovascular risk. Clinical Considerations Reduce levels of oxidative stress, such as free radical exposure and alcohol intake as these can further impair the MAT1A enzyme. Ensure adequate levels of MAT1A cofactors such as magnesium and potassium. Consider testing RBC magnesium and potassium. Patients with this polymorphism may have higher homocysteine in response to dietary fat intake than those without. Monitor advanced cardiovascular risk markers if clinically appropriate. Glycine, supporting ATP production may support the production of SAMe.

PMID: 20335551, 22496743, 21185701

MTR

Methionine Synthase catalyzes the re-methylation of homocysteine to methionine using a methyl group donated by 5-methyltetrahydrofolate.

Cofactors: Zinc & vit B12

Epigenetic Control Points

Inhibitors

Ar, Cd, Pb, Hg, Al

Nitrous oxide, Nitric oxide

Inflammation, ROS, H2O2 (oxidative stress)

Reduced levels of Glutathione & B12

Increased level of Acetaldehyde

Nitrates/nitrites (processed meat)

Excess Copper

Inducers

Reduced SAM

Reduced Methionine

Increased Dopamine

SNP: rs1805087

Genotype: AG

G allele is associated with increased activity & lower homocysteine levels. (excessive or altered DNA methylation). Intermediate risk for male Infertility, Autism, Depression & Stress, Cognitive impairment. Negative or mixed Association with NTDs/Congenital heart disease/CVDs and Cancer.

SNP: rs3768142

Genotype: GG

slow enzymatic activity; reduced risk of ventricular septal defect and non-syndromic cleft lip/ palate in the offspring; but increased risk of agranulocytosis on methotrexate.

Interpretation & Actionable Insights

This SNP upregulates the MTR enzyme leading to lower homocysteine levels. Its polymorphism is associated with Congenital birth defects like Spina bifida, Cleft lip/palate & Cardiac defects. MTR enzyme is at the junction between the folate pathway and the methylation pathway, upregulation of MTR may shunt folate groups to the methylation cycle at the expense of other folate needs, such as purine/nucleotide synthesis.

PMID: 11257268, 28094822, 37249073, 25625218, 31969693

MTRR

Methionine synthase reductase supports the function of Methionine synthase, which turns homocysteine into methionine with the help of active folate. This pathway relies on active vitamin B12.
MTRR restores oxidized Cobalamin to CH3-Cobalamin in order to maintain the MTR activity.

Cofactors: SAM, FAD, NAD
vit B12, Zn

Epigenetic Control Points

Inhibitors

- Oxidative stress
- Mercury
- Cadmium
- Industrial solvents
- Excessive EMF exposure

Inducers

- IGF-1
- Dopamine
- Folate
- Vit B12
- SAMe
- Omega-3
- Flavonoids

SNP: rs1801394

Genotype: AG

Slightly lower activity.
G allele – lower affinity of MTRR for MTR
Impaired response to folate supplementation for Hcy reduction
Male fertility issues (Asians) & ADHD in children

SNP: rs1532268
Genotype: CT

T allele reduces the enzyme function; T allele is associated with increased homocysteine when B12 status is low.
Associated with increased risk of VSD (Ventricular Septal Defect) and Schizophrenia
It is also linked to Gastric cancer, Congenital heart disease & NTDs.

Interpretation & Actionable Insights

A66G (1801394) : Elevates Hcy independent of folate, vit B12 & B6 levels. Increased Choline needs. Birth defects & NTDs could occur when cobalamin status is low or when MTHFR C677T is present. Down syndrome, VSD. Higher risk for meningioma. It correlates with global DNA hypomethylation, which is a direct marker for methylation impairment. Clinical considerations: Compare any MTRR polymorphisms with MTHFR and MTR genetic results Evaluate homocysteine, SAM/SAH ratio, and monitor biomarkers for vitamin B-12 and folate. Ensure adequate dietary intake of folate and vitamin B-12, consider repletion with methylcobalamin in these individuals. Ensure adequate vitamin B-2 and B-3 status, as they are cofactors for the MTRR enzyme. Assess antioxidant capacity, as oxidative stress impacts levels of methylcobalamin

PMID: 11472746, 24748989

MTHFR

MTHFR (Methylene Tetra Hydro Folate Reductase) produces body's primary form of folate (methyl folate-80% of total folate level). It is the rate limiting step, both in the generation of 5-MTHF & SAMe.
5-MTHF is utilized in the production of SAMe which in turn regulates 200 processes including DNA methylation, neurotransmitter & phospholipid production.
The MTHFR gene connects the folate pathway, via 5-MTHF with the SAM cycle via the MTR gene.

Cofactors: FAD, NADPH (Vit B2)

Epigenetic Control Points

Inhibitors

Arsenic, Lead, Mercury

Thyroid issues, Insulin resistance

Food or beverages enriched with folic acid

Folic acid, Aspirin, NSAIDs

Increased SAM

Alcohol, Smoking, Excess Sulfur

Inducers

Vitamin B2 (cofactor)

Conditions:

Low Methionine,
Reduced SAM:SAH ratio

B6, B9, B12, TMG, Mg

SNP: rs1801131

Genotype: TG

Slightly reduced activity

SNP: rs1801133

Genotype: GG

Typical

Interpretation & Actionable Insights

Your Story with MTHFR: You usually don't eat leafy greens everyday You can focus and concentrate well You are often tired and toxic You may have exercise induced asthma You are likely to have shortness of breath/ red face after exercising You have fluctuating moods between irritability and depression. You cannot tolerate alcohol easily N2O (Laughing gas) at the dentist or doctor's office makes you horrible Treat Hypothyroidism if present: Support thyroid function with low stress, sleep, adrenal support, Healing gut, avoiding chemicals, filtering water and fighting off infections. Supplements: B2 (20-400 mg/day) L-5-MTHF 400 mcg and then dose up No or poor response to methyl folate may be due to Folate Receptor Ab Folic acid B12 deficiency (Folate trap) D-methyl folate supplements Heavy metals Oxidative stress Infections/Meds Living in sunny areas and over exposure leads to increased folate demand to repair sun-damaged skin. Naturally dark skin can reduce demand, but not entirely. Riboflavin rich, choline and betaine rich , natural folate rich, polyphenol rich supports its function. Supplements: 5-MTHF may be useful. Consider lower amounts 400-1000 mcg to avoid side effects. Most

Interpretation & Actionable Insights

importantly, C677T polymorphisms respond very well to high doses of Vit B2 with adequate folate supply. Creatine & Phosphatidyl choline (non-GMO, sunflower derived) conserve SAM and generate less homocysteine. Consider calcium, betaine, omega-3, ALA & DHA. Vit C decrease hypermethylation of MTHFR in a positive way. Consider more folinic acid, L-5-MTHF or Choline during prolonged sun exposure, during pregnancy and breast feeding.

METHYLATION PEARLS:

Excess alcohol consumption depletes B vitamins and increases the risk of Choline deficiency. It can also worsen the impact of your genetics by blocking MTR & PEMT. It may even increase the risk of different congenital disorders like Fetal Alcohol Spectrum Disorders (FASD). Alcoholics and lactating women are at risk of folate deficiency. Methyl-cobalamin is the active form of B12, suitable in poor methylation. Active B complex along with omega-3 lowers Hcy, suitable for people at risk of dementia or heart disease. SAMe supplementation may help with Joint pain, Liver disease & Depression.

SAM-e may not be safe in Bipolar disorder as it interacts with 5-HTP, St. John's wort, and different medications. Combining it with anti-depressants can be life-threatening. Never take SAM-e supplements without consulting your doctor.

Extreme exercise may contribute to heart rhythms, irregular periods, and more.

Zn is important for folate absorption, its role and healthy methylation.

Creatine may help reduce your requirements for methylation, especially if you have high Hcy.

The Common Barriers to Optimal Methylation are as follows:

1. GI dysbiosis

2. Increased oxidative stress

3. Poor stress management

4. Exposure to environmental toxins

5. Nutritional insufficiencies

6. Poor sleep

7. Medications (antacids, NSAIDs, glucocorticoids)

Avoid Exposure to heavy metals helps with methylation.

Avoid BPA (Bisphenol A) Exposure as it demands methylation for detox and glutathione for neutralization.

People with methylation issues may have increased needs for B vitamins & Choline, the deficiencies of which may lead to liver dysfunction, NTDs and more.

BHMT is primarily found in liver & kidneys. Avoid High Dose Niacin supplements (>500 mg may lower T4-mediated through TBG). Niacin in large amounts can deplete methyl donors like SAMe.

Beetroot naturally contains betaine (TMG) which acts as a methyl donor in the body. TMG supplementation (1.5-4 g/day) for 2-6 months may lower HCY levels. Doses above 4g/day may increase LDL & Triglycerides levels. Direct or functional (genetic polymorphisms & alcohol intake) Vit B12 deficiency: MTR cannot convert Hcy to Methionine NOR can it return 5-MTHF to THF for use in Folate cycle.

Supplementation with methylated folate may be ineffective for patients with poor B12 status.