Welcome to your Methylation report!

You've taken a great step on your personalised wellness journey by exploring the science of methylation.

Understanding your body's unique needs is key to long-term wellness. Methylation, a critical biochemical process influenced by your genetics, plays a pivotal role in numerous bodily functions.

Your Methylation report will reveal how your unique genetic makeup affects your methylation capabilities, guiding you in optimising your nutrient intake for enhanced methylation activation. This personalised insight empowers you to tailor your lifestyle and nutrition choices to boost your overall health and wellbeing.

Within your report, you'll discover the importance of key nutrients in methylation, how your DNA impacts your needs, and actionable steps to optimise your methylation pathways.

Read on to find out more about you.

What is Methylation?

Methylation refers to the process of transferring methyl groups between molecules, altering their structure and function. A methyl group is made up of one carbon atom and three hydrogen atoms (-CH3), hence the alternative term "one carbon metabolism". In biological systems, it primarily involves the addition of a methyl group to DNA, RNA, or proteins. The process plays a critical role in regulating gene expression, protein function and cellular processes, and occurs billions of times each second throughout our bodies. Understanding methylation and its impact on health is crucial for managing and optimising these vital biochemical processes. Genetic variations in key genes involved in the methylation cycles can significantly influence individual health outcomes, necessitating personalised approaches to nutrition and supplementation.

Methylation is essential for a multitude of processes within our body, without which we simply wouldn't function. The regulation of gene expression, energy production, fat metabolism, protein function, immune responses and cell membrane repair all rely on methylation. Additionally, methylation plays a key role in the production and metabolism of neurotransmitters that regulate mood (and other neural processes) and so has a huge impact on our mental function. It also aids in detoxification processes that neutralise toxins, thereby promoting overall health.

What factors can influence our methylation capabilities?

Several factors can impact methylation, including diet, toxin exposure and stress. Deficiencies in key dietary cofactors such as vitamins and minerals can impair the methylation process. In turn this can increase susceptibility to chronic conditions such as impaired immunity, fatigue, cardiovascular disease, neurological disorders, multiple cancers, and mood and psychiatric disorders.

How do our genes affect Methylation?

We all carry genes that are involved at various stages within the methylation pathways, and variants in these genes can significantly influence their function. By assessing these genetic variants, or single nucleotide polymorphisms (SNPs), we can understand their potential impact on how that gene functions and identify any inhibited methylation pathways. In turn, this can help us identify an individual's specific nutritional support needs or lifestyle interventions which could reduce potential risks and contribute to better overall health. Although you can't change your genetic code, the expression, synthesis, and function of your genes can be modulated and supported once we are armed with the right knowledge!

Helpful Terms

You'll see some of the same terms come up many times throughout your report. Here are some definitions you can refer back to:

Methylation

A biochemical process involving the transfer of methyl groups between molecules, crucial for regulating gene expression, protein function, and detoxification. Methylation occurs billions of times per second in every cell. Impaired methylation can lead to health issues such as cardiovascular disease, neurological disorders and impaired detoxification, while overactive methylation can cause abnormal gene expression and potentially cancer.

One Carbon Metabolism

Another name for methylation, so-called because the process involves transferring one carbon and three hydrogen atoms to another molecule.

Methyl Group

A chemical group consisting of one carbon atom bonded to three hydrogen atoms (CH3). Methyl groups are transferred between molecules in methylation reactions, influencing gene expression, protein function, and metabolism. Imbalances can disrupt numerous biological processes.

Homocysteine

A sulphur-containing amino acid that is an intermediate product in the metabolism of methionine and cysteine. Elevated levels of homocysteine, known as hyperhomocysteinaemia, can increase the risk of cardiovascular diseases, cognitive decline, and other health issues. Low levels are uncommon and usually not problematic, but they may indicate a deficiency in related nutrients such as folate or vitamin B12.

Methionine

An essential amino acid obtained from dietary protein that plays a key role in methylation. Methionine is converted to S-adenosylmethionine (SAMe), the body's primary methyl donor. Deficiency can impair methylation and detoxification processes, while excess methionine intake can lead to elevated homocysteine levels, increasing the risk of cardiovascular diseases.

SAMe (S-adenosylmethionine)

A compound derived from methionine and ATP that serves as the primary methyl donor in numerous biochemical reactions, including DNA methylation, neurotransmitter synthesis, and detoxification. Low levels can impair these processes, while high levels may indicate excess methionine intake or dysregulated methylation.

SAH (S-adenosylhomocysteine)

A byproduct of methylation reactions where SAMe donates a methyl group. SAH is subsequently hydrolysed to homocysteine and adenosine, and high levels of SAH can inhibit methylation. Elevated SAH can indicate impaired methylation and contribute to elevated homocysteine levels.

SAMe:SAH Ratio

The SAMe:SAH ratio is commonly used as an indicator of cellular methylation potential. A higher ratio suggests a favorable environment for methylation reactions, implying that there are sufficient methyl groups available. Conversely, a lower ratio may indicate a reduced capacity for methylation, possibly due to lower levels of SAM or higher levels of SAH.

Cofactors

Non-protein chemical compounds that bind to enzymes and are necessary for their activity. Cofactors can be metal ions (such as magnesium or molybdenum) or organic molecules (such as vitamins). Deficiency in cofactors can impair enzyme function, while excessive intake can sometimes disrupt metabolic balance.

Neurotransmitters

Chemical messengers that transmit signals across synapses between neurons and other cells. Key neurotransmitters include serotonin, dopamine, norepinephrine, and acetylcholine, which play vital roles in mood regulation, cognition, and bodily functions. Imbalances can lead to mental health issues, while normal levels are crucial for healthy brain function.

Neurotransmitter Metabolism

The processes involved in the synthesis, release, reuptake, and breakdown of neurotransmitters. Proper metabolism is essential for maintaining neurotransmitter balance and function, which affects mood, cognition, and overall neurological health. Disruptions can lead to neurological and psychiatric disorders.

Oxidative Stress

A state where there is an imbalance between the production of free radicals (like superoxide radicals) and the body's ability to detoxify them with antioxidants. This imbalance can lead to cellular damage, inflammation, and contribute to various diseases, including cardiovascular and neurodegenerative disorders. Managing oxidative stress is essential for maintaining overall health.

Free Radicals

Highly reactive molecules with unpaired electrons that can cause cellular damage through oxidative stress. Free radicals are produced during normal metabolic processes and in response to environmental factors. Excessive free radicals can lead to chronic diseases, while very low levels may affect normal cellular signalling.

Superoxide Radicals

A type of free radical formed when oxygen gains an extra electron. Superoxide radicals are highly reactive and can damage cellular components, contributing to oxidative stress and inflammation. High levels are harmful, while very low levels might impair certain cell signalling pathways.

Atheroprotective

Refers to substances or actions that protect against the development of atherosclerosis, the buildup of fatty plaques in the arteries that can lead to cardiovascular disease. Lack of atheroprotective factors can increase cardiovascular risk, while enhancing these factors can improve heart health.

Vasodilation

The widening of blood vessels, which decreases blood pressure and improves blood flow. This process is mediated by various factors, including nitric oxide, and is important for maintaining cardiovascular health. Impaired vasodilatation can lead to hypertension and cardiovascular disease, while excessive vasodilatation can cause dangerously low blood pressure.

Vitamin B9

An essential B vitamin encompassing both folate and folic acid, crucial for numerous metabolic processes including DNA synthesis and repair, and methylation.

Folate

The natural form of vitamin B9 found in food sources such as leafy greens, legumes, and fruits. It is involved in DNA synthesis and repair, and the conversion of homocysteine to methionine. Deficiency can lead to anaemia and neural tube defects, while excess intake from supplements may mask vitamin B12 deficiency.

Folic Acid

The synthetic form of vitamin B9, commonly found in supplements and fortified foods. It needs to be converted to its active forms (methylfolate) in the body. High intake of folic acid can potentially mask a vitamin B12 deficiency, and lead to a variety of possible health risks.

Cobalamin

Another name for vitamin B12, an essential vitamin that plays a crucial role in the methylation of homocysteine to methionine, red blood cell formation, and neurological function. Deficiency can cause anaemia and neurological disorders, while high intake is generally considered safe as excess is excreted.

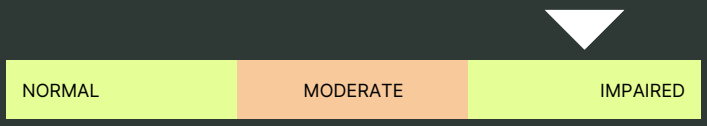
Molybdenum

A trace mineral that acts as a cofactor for several enzymes, including those involved in the detoxification of sulphite and the metabolism of certain amino acids. Deficiency is rare but can lead to metabolic disturbances, while excessive intake may cause toxicity.

The Folate Cycle

The Folate Cycle

Your Folate Cycle results show an Impaired Efficiency



Gestational/Pregnancy health

DNA synthesis and repair

Energy production

Inflammation control

Detailed Summary

The Folate Cycle is the first stop for the folate (vitamin B9) that enters our bodies. It is here that we convert folate into usable forms for numerous important processes occurring elsewhere in the body, including the other pathways detailed later in this report.

Dietary folate naturally occurs in foods like leafy greens, legumes, and liver. Folate can also enter our bodies in the form of synthetic folic acid, which is found in supplements and added to fortified products. After absorption in the small intestine, the folate is transported to our cells where vitamin B3 is used to convert it into dihydrofolate (DHF) and then tetrahydrofolate (THF).

There are then two potential destinations for folate entering the folate cycle: it can be utilised as part of the methylation process that facilitates DNA formation during cell division, or alternatively it is converted to methylfolate (5-MTHF), which is the "active" form of folate. This process happens in the cells of the liver and other tissues. The process of producing these metabolites is sequential and reversible depending on the body's needs, and relies on vitamins B3 and B6.

Among other things, methyl groups donated from 5-MTHF are a critical part of the methionine cycle - supporting the conversion of homocysteine to methionine. This process also requires vitamin B12 and zinc. Furthermore, 5-MTHF also helps regenerate BH4 from BH2, which is essential for producing neurotransmitters like dopamine and serotonin.

Considerations

Depending on your results and current diet, it may be important to pay particular attention to your intake of B vitamins - especially B9, B2, B3, and B6. If supplementing, methylated forms (e.g. 5-MTHF) may be more effective, particularly if your folate cycle is genetically impaired at all. Testing folate levels via a blood test can provide insight into your folate status; a serum folate marker reflects recent intake, whereas a red blood cell folate test indicates longer-term folate status.

Key Genes

DHFR - This gene helps assimilate folate from both dietary and supplemental sources, and is involved in converting DHF to THF. THF functions as a methyl group carrier and is essential for DNA synthesis, and is also needed to make 5-MTHF, the active version of folate. The deletion variant of this gene impacts folic acid metabolism, which can reduce the availability of 5-MTHF. In these individuals, high folic acid intake of more than 500mcg per day can lead to unmetabolised folic acid in the blood, while chronically low intakes (250mcg) are associated with low red blood cell folate levels.

MTHFD1 - This gene encodes an enzyme that supports the reactions involved in the processing of folate-derived compounds. These reactions help convert one-carbon units attached to THF into forms needed to support the synthesis of purines (for DNA synthesis and repair) and thymidine (for nucleotide biosynthesis), and also supply methyl groups for methionine generation. Variants in this gene can influence how effectively these pathways function.

MTHFR - This gene provides instructions for making an enzyme that plays a crucial role in processing folate and maintaining proper levels of homocysteine. The MTHFR enzyme converts 5,10-methylenetetrahydrofolate into 5-MTHF. This form is critical for DNA synthesis and repair as well as numerous other methylation reactions. 5-MTHF is also required to convert homocysteine into methionine, an essential amino acid. Elevated homocysteine levels, common when MTHFR function is impaired, can increase the risk of cardiovascular disease and pregnancy complications amongst other things. There are two variants assessed here: C677T variants can directly impact 5-MTHF (and therefore homocysteine) levels, whereas A1298C variants can impact the functioning of the BH4 and urea cycles.

MTR - This gene encodes an enzyme that uses 5-MTHF to convert homocysteine into methionine. The enzyme requires vitamin B12 (methylcobalamin) to function properly. Without adequate B12, the cycle can become impaired, leading to elevated homocysteine and reduced methionine availability.

Your Genetic Results

The below table shows the genes analysed in relation to your Folate Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
DHFR	rs70991108	DD	●●
This variant can impact enzyme activity, which can affect folic acid metabolism and result in depleted 5,10-methylene-THF and therefore 5-MTHF. High folic acid intakes (>500mcg/day) can result in high levels of plasma unmetabolised folic acid, whereas low intakes (250mcg/day) can lead to low red blood cell folate.			
MTHFD1	rs2236225	CT	●
This genotype may result in reduced gene activity. This can reduce the supply of methylfolate to The Methionine Cycle and potentially increase dependency on 'shortcut' route homocysteine recycling, impacting betaine and its substrate choline.			
MTHFR (A1298C)	rs1801131	AA	-
This genotype is not associated with reduced MTHFR enzyme activity. You do not carry the genetic mutation that can impact BH4 levels.			
MTHFR (C677T)	rs1801133	TT	●●
This variant is associated with a 70% reduction in MTHFR enzyme activity. About 30% of the population possess at least one T allele, and it is associated with an increased risk of high homocysteine & low folate levels.			
MTR	rs1805087	AA	●●
You do not carry an "upregulating" allele for this gene, meaning lower MTR function and potentially higher homocysteine levels than carriers of the G allele.			

Specific Gene Advice

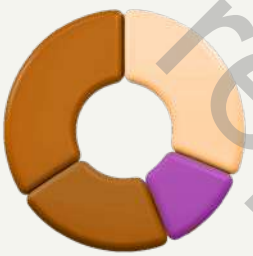
Based on specific gene results we also have the following recommendations:

Gene	Recommendation
DHFR	Monitor your intake of (unmethylated/unreduced) folic acid, as high intakes (over 500mcg/d) can lead to high levels of circulating unmetabolised folic acid and further increase enzyme activity, which has been associated with potential health risks. Ensure adequate intake of reduced form folate, which can be found in foods such as green leafy veg and citrus, or reduced form supplements such as methylfolate (e.g. 5-MTHF) as these are the "active forms" and will be more readily utilised.
MTHFD1	Folate insufficiency is a possible result of carriers of your genotype, so ensure intake is adequate. It is also advisable to check betaine & choline levels, as these can become depleted. Choline depletion may increase risk of endometriosis in females, and related infertility.
MTHFR (C677T)	Support your MTHFR activity by increasing your intake of vitamin B-rich foods such as dark leafy greens. If supplementing, vitamins B9 (folate), B2 (riboflavin) and B3 (niacin) are important. Active versions (e.g. 5-MTHF) are more readily utilised. Monitoring levels of these vitamins as well as homocysteine, SAM and SAH (see The Methionine Cycle) is advisable.
MTR	It is important to consider your MTR result in conjunction with MTHFR to assess overall impact as this result with a reduced MTHFR enzyme activity can lead to high levels of homocysteine. As your genetic result is associated with elevated homocysteine levels, consider monitoring this as well as folate and vitamin B12 levels.

Advice for you

Here's some recommended lifestyle tips and practices based on your result

With these genetic results it is important to consider your intake of all B vitamins - paying particular attention to vitamins B9 (folate) B2, B3 and B6. Look for methylated forms (e.g. 5-MTHF for folate) as these are the "active forms" and will be more readily utilised.



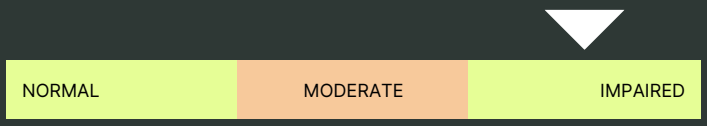
Blood testing is a great way to monitor potential risks associated with methylation - homocysteine levels, SAMe:SAH ratio and B vitamin levels are useful markers to track.

If taking a blood test, pay attention to folate levels. Serum folate levels can be easily affected by recent intake (dietary or supplementary) and so erythrocyte (red blood cell) folate levels may be a better indicator of tissue status.

The Methionine Cycle

The Methionine Cycle

Your Methionine Cycle results show an Impaired Efficiency



Gestational health Amino acid synthesis Metabolic health

Detailed Summary

The Methionine Cycle is one of the body's key biochemical processes, involving some of the most well-studied methylation genes. One of its main products is SAMe, which donates methyl groups needed for many important reactions in the body.

Methionine is first converted into S-adenosyl-methionine (SAMe), a transformation that uses ATP for energy, as well as magnesium. This step depends on an enzyme called MAT1A; variations in this gene can influence how well this conversion happens, and in turn how well your body can perform methylation. Once formed, SAMe acts as the body's primary methyl donor, enabling processes such as DNA repair, neurotransmitter production and detoxification. After donating its methyl group, SAMe becomes S-adenosyl-homocysteine (SAH). It's important to keep SAH levels under control, as too much can slow down methylation.

Next, the by-product homocysteine is recycled back into methionine. This happens through two pathways: a vitamin B12 and folate-dependent route involving an enzyme called MTR, and a betaine-dependent route involving the enzyme BHMT. This recycling process also supports the body's supply of choline, which plays a role in liver health and brain function.

Homocysteine either continues cycling through this process or is diverted to the Transsulphuration Pathway.

Considerations

When assessing The Methionine Cycle, it may be helpful to measure folate and vitamin B12 levels. Homocysteine methionine status may also be considered.

Key Genes

MTR - This gene encodes methionine synthase, an enzyme that catalyses the remethylation of homocysteine to methionine via the 'long route', using 5-methyltetrahydrofolate (5-MTHF) from The Folate Cycle as a methyl donor, resulting in the formation of methylated vitamin B12 (methylcobalamin).

MTRR - This gene is responsible for regenerating MTR via a methylation reaction that utilises SAMe as a donor. Additionally, MTRR aids in maintaining MTR activity by recycling and converting vitamin B12 to its methylated form (methylcobalamin).

FUT2 - This gene influences the presence of specific carbohydrate markers - H antigens - in the gut lining, which in turn determines an individual's secretor status. The absorption of vitamin B12 depends on the secretion of the glycoprotein intrinsic factor (IF) by gastric cells, the binding of IF to vitamin B12, and a functional gastrointestinal absorption system.

TCN2 - This gene encodes transcobalamin II, a protein responsible for binding and transporting vitamin B12 into cells.

PEMT - This gene encodes an enzyme that transforms phosphatidylethanolamine into phosphatidylcholine through a series of methylation steps in the liver, helping the body maintain adequate choline levels. Oestrogen plays a regulatory role by enhancing PEMT gene activity, giving premenopausal women a greater capacity to make choline internally than postmenopausal women or men.

BHMT - This gene encodes an enzyme that facilitates the remethylation of homocysteine to methionine through the 'short route', utilising betaine as a methyl donor upon conversion to DMG (dimethylglycine). The BHMT pathway relies on zinc and requires sufficient levels of TMG (trimethylglycine or betaine) for optimal functioning. This process is essential for the irreversible oxidation of choline. BHMT activity may also be influenced by cortisol levels (stress) and could potentially impact norepinephrine levels, thereby contributing to ADD/ADHD.

Your Genetic Results

The below table shows the genes analysed in relation to your Methionine Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
MTR	rs1805087	AA	●●
You do not carry an upregulating allele for this gene, which is associated with lower MTR function and potentially elevated homocysteine levels. This can in turn reduce methionine levels, which can influence cancer risk and tumor growth, as approximately 50% of cancer cell types depend on methionine.			
MTRR	rs1801394	AG	●
You carry one copy of the G allele, which downregulates the activity of the MTRR gene and reduces the ability to re-methylate the vitamin B12 needed for MTR to function in the methionine cycle. This can contribute to high levels of homocysteine.			
BHMT	rs3733890	AG	●
You carry one copy of the A allele which has been linked to reduced BHMT function. This can negatively impact the betaine-based route for converting homocysteine to methionine. As a result, levels of homocysteine may rise, which has been associated with an increased risk of neural tube development issues.			
PEMT	rs7946	CT	●
Your genotype is linked with reduced PEMT function, which may lower the body's ability to synthesise choline. This can in turn affect betaine production, which is important for the BHMT-driven recycling of homocysteine. Reduced PEMT function may have a more pronounced effect in men and postmenopausal women due to lower oestrogen levels.			
FUT2	rs601338	GG	●●
You carry two copies of the G allele, which indicates an active FUT2 gene and secretor status. This increases susceptibility to H. pylori infection and gastritis linked to reduced B12 absorption.			
TCN2	rs1801198	CG	●
Your genotype is associated with the downregulation of TCN2, resulting in lower cellular and plasma levels of transcobalamin, the carrier protein responsible for transporting vitamin B12 to cells. This association has been observed in developmental disorders and pregnancy loss, though it doesn't seem to affect homocysteine levels.			

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

Gene	Recommendation
MTR	Take into account both your MTR and MTRR results to evaluate the overall effect on your vitamin B12 levels. Since your genetic results are linked to elevated homocysteine levels, consider monitoring this. You can support MTR activity by supplementing with the methylated form of vitamin B12 (e.g. methylcobalamin).
MTRR (A66G)	Hydroxycobalamin (the injectable form of vitamin B12) may be the preferred form for this result. Additionally, maintain sufficient antioxidant intake with foods like berries, kale, and various herbs and spices to reduce oxidative stress. Support methylation with B2 from foods such as eggs, almonds, and spinach, and B3 from foods like chicken, peanuts, and brown rice. Both smoking and secondary exposure to tobacco smoke should be avoided, as smoking is known to increase homocysteine levels.
BHMT	To support this pathway, it may be beneficial to consume more nutrients such as zinc (e.g. from meat, legumes, and seeds), betaine (from foods like spinach & beetroot), and choline (found in eggs), which serves as a precursor to betaine.
PEMT	Ensure adequate dietary intake of choline found in eggs, beef, chicken and fish.
FUT2	Due to your gene result, you have an elevated risk for vitamin B12 deficiency. It is, therefore, important for you to meet the RDA for vitamin B12 (2.4 mcg daily) by consuming foods like fish, meat, poultry, eggs, dairy products, and nutritional yeast. If you struggle to meet this RDA, consider a supplement. Opt for the methylated forms of B12 (e.g. methylcobalamin) as it'll be better utilised.
TCN2	To support gastrointestinal health, incorporate probiotics into your diet from foods like kefir or kimchi, or through supplementation, and increase your fiber intake with legumes, grains, fruits, and vegetables. Additionally, consider supplementing with methylated vitamin B12 (e.g. methylcobalamin).

Advice for you

Here's some recommended lifestyle tips and practices based on your result

With these genetic results it is important to consider your intake of folate (green leafy veg), vitamin B12, betaine (beetroot) and choline (eggs). If supplementing, methylated folate and B12 (methylcobalamin) is recommended. SAMe supplementation may be considered.

Functional testing of homocysteine, methionine, vitamin B12 and SAMe levels may be considered. Zinc levels may also be indicative. The ratio of SAH: SAMe is also a useful indicator of SAMe conversion.

Prioritising your gastrointestinal health by integrating probiotics into your diet—whether through foods like yogurt, kefir, kimchi or sauerkraut or via supplementation—and increasing fiber intake from sources like legumes, grains, fruits, and vegetables is advantageous.

The Transsulphuration Pathway

The Transsulphuration Pathway

Your Transsulphuration Pathway results show a Normal Efficiency

Oxidative stress reduction

Vascular/circulatory functioning

Neuroprotective roles

Telomere protection

Detailed Summary

The Transsulphuration Pathway is a metabolic process that offers an alternative pathway for the conversion of homocysteine where it is converted to cysteine via the intermediate cystathionine. Cysteine is a precursor of glutathione (a major antioxidant), and taurine (an essential amino acid). Cystathionine is also a central component of sulphur metabolism. This involves the oxidation of sulphite, which is produced from cystathionine, to sulphate and is catalysed by a molybdenum-dependent enzyme, helping to detoxify sulphites in the body. Sulphites can increase cortisol and cause brain fog while sulphate is less toxic and can be excreted in the urine.

Once homocysteine is converted to cystathionine, it is then converted into cysteine which requires vitamin B6 as a co-factor. This conversion process generates ammonia (which in large amounts can deplete BH4 - see The BH4 Cycle) as a by-product. Glutathione synthesis in the liver is dependent upon the availability of cysteine and is important for healthy detoxification as well as protecting cells from oxidative damage by free radicals, detoxifying xenobiotics, and facilitating membrane transport. Cysteine can also be further converted into taurine through a series of enzymatic reactions. Taurine is an important amino acid that plays various roles in bile salt formation, cellular osmoregulation, and neurotransmission. The pathway also involves the creation of succinyl-CoA, a reaction that depends on adenosylcobalamin (vitamin B12) as a cofactor. Succinyl-CoA is a critical intermediate in The Krebs Cycle and is crucial for the synthesis of ATP, heme, cytochrome P450s, and nucleotides.

Considerations

To explore how well the Transsulphuration Pathway is functioning, measuring key metabolites involved in the process (such as cystathionine, cysteine and homocysteine) can help. Measuring folate vitamin B12 can also provide insight into overall methylation functioning.

Key Genes

CBS - this gene encodes an enzyme responsible for the first step in the Transsulphuration Pathway. The cystathionine beta-synthase (CBS) enzyme helps convert homocysteine into cystathionine. This conversion depends on the availability of vitamin B6 and iron (as heme).

GSS - This gene encodes an enzyme that governs the later stage of glutathione production. It converts cysteine into glutathione in a reaction that depends on ATP for energy.

Your Genetic Results

The below table shows the genes analysed in relation to your Transsulphuration Pathway Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
CBS	rs234706	AG	●
This genotype slightly upregulates CBS gene activity and can "pull" more homocysteine from The Methionine Cycle into The Transsulphuration Pathway. Therefore, this result is associated with lower homocysteine levels and can counteract inhibited MTHFR activity. However, this can reduce SAMe synthesis, deplete vitamins B6 & B12, and may also lead to low glutathione production.			
GSS	rs6088659	CC	-
Your results indicate that your GSS enzyme function is typical and should support normal glutathione synthesis. However, if ATP levels are low - regardless of genotype - this can limit the enzyme's ability to carry out this process efficiently.			

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

Gene	Recommendation
CBS (C699T)	Support healthy ammonia levels by supporting gut health and muscle mass. Bifidobacterium and Lactobacillus bulgaricus may help to reduce ammonia levels (found in Stride's GS-01 supplement). Supporting muscle mass with strength and resistance training can buffer ammonia by converting it to glutamine. Food sources of arginine (poultry, pumpkin seeds, soy) and citrilline (watermelon, cucumber) may also support excretion of ammonia. Ensure adequate intake of vitamins B6 and B12.
GSS	Regardless of your genotype, low ATP levels can affect GSS and therefore glutathione synthesis. You can assist your body's ATP production by consuming fatty acids and protein from lean meats like chicken and turkey, fatty fish like salmon and mackerel, and nuts.

Advice for you

Here's some recommended lifestyle tips and practices based on your result

Although genetically your Transsulphuration Pathway is working efficiently, it is still important to ensure sufficient intake of vitamins B2, B6, B12, choline, zinc, and betaine.

Animal proteins and by-products such as beef, chicken, fish, eggs, and milk are excellent sources of vitamins B2, B6, B12, choline, and zinc, although excessive intake can elevate ammonia levels. Betaine can be found in beetroot, green leafy vegetables, and wholegrains like quinoa.

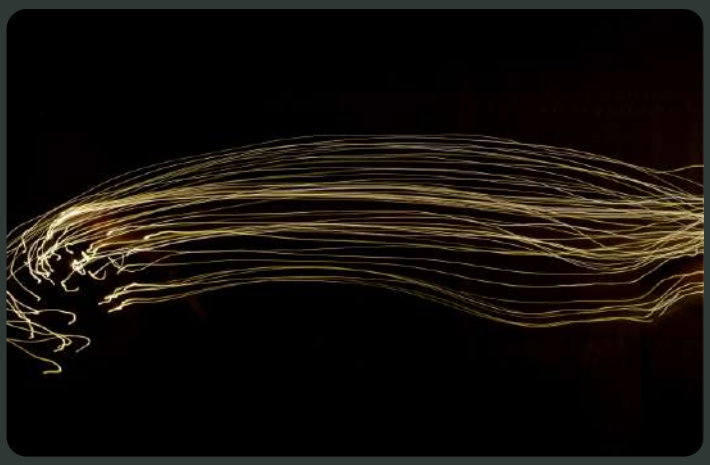
Urine and plasma amino acid profile testing is a great way to monitor potential risks associated with homocysteine metabolism. It may be beneficial to check levels of homocysteine, taurine, glutathione, ammonia, and sulfur-containing amino acids such as cysteine and methionine.

The BH4 Cycle

The BH4 Cycle

Your BH4 Cycle results show a Moderate Efficiency

NORMAL	MODERATE	IMPAIRED



Neurotransmitter metabolism Thyroid health Inflammation Oxidative stress

Detailed Summary

The BH4 Cycle is essential for various processes in the body, including neurotransmitter metabolism, specifically in the production of key neurotransmitters such as dopamine, serotonin, melatonin, norepinephrine, and thyroid hormones.

In this cycle, BH4 or Tetrahydrobiopterin is regenerated from dihydrobiopterin (BH2). An enzyme catalyses the regeneration of BH4 from BH2, a reaction requiring active folate (5-MTHF) from The Folate Cycle. Phenylalanine is converted to tyrosine with the help of BH4. Tyrosine is then converted into a precursor of dopamine and subsequently into dopamine itself, with BH4 acting as a crucial cofactor in this process. Similarly to tyrosine, tryptophan is converted into a serotonin precursor, and then into serotonin, again requiring BH4. Serotonin is then oxidised into melatonin, a process that requires SAMe from The Methionine Cycle and vitamin B2 as cofactors. Norepinephrine from dopamine is converted to epinephrine in the adrenal medulla, also requiring SAMe as a methyl donor. BH4 also contributes to the Urea Cycle and plays a role in detoxification by supporting the conversion of ammonia into a less harmful form. It is also needed for nitric oxide production. Imbalances or heightened sensitivity to neurotransmitter levels can be linked to issues such as mood swings, irritability, disrupted sleep, and concentration difficulties.

Considerations

When investigating the efficiency of The BH4 Cycle, testing your neurotransmitter balance and SAH:SAMe ratio could be beneficial. Assessing the amino acids tryptophan and tyrosine, vitamins B2, B6 and D, and methylfolate levels is also helpful. Environmental factors can also have a strong effect: stress both physical and mental, and diet (e.g., stimulants or toxicity of heavy metals).

Key Genes

VDR - This gene encodes the nuclear hormone receptor for vitamin D3 (the active form of vitamin D in the body). This catalyses the conversion of tyrosine into dopamine.

COMT - This gene plays a role in the metabolism of dopamine, noradrenaline, and adrenaline. These neurotransmitters play significant roles in regulating mood, cognition, and the body's response to stress.

MAOA - this enzyme is involved in breaking down neurotransmitters including serotonin, melatonin, noradrenaline, and adrenaline. Because the MAOA gene is found on the X chromosome, males only inherit one copy, which can affect how we interpret their results. For this reason, male genotypes are described as hemizygous.

MAOB - this gene codes for an enzyme responsible for degrading compounds such as phenethylamine, benzylamine, histamine and dopamine. Just like MAOA, MAOB is found on the X chromosome, hence males possess only one allele inherited from their mother.

MTHFR - A key regulatory enzyme responsible for converting folate to its "active" form: 5-MTHF (methylfolate). The particular SNP looked at here (A1298C) regulates the conversion of MTHF to BH4 which is vital in the metabolism of neurotransmitters, phospholipids and proteins.

Your Genetic Results

The below table shows the genes analysed in relation to your BH4 Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
MTHFR (A1298C)	rs1801131	AA	-
This allele result is associated with normal BH4 levels needed for neurotransmitter synthesis. Methylfolate is pulled from the methionine cycle more readily, so ensure folate levels are adequate to support this and avoid negatively impacting homocysteine recycling.			
COMT	rs4633	CC	-
You carry alleles associated with normal COMT activity, resulting in normal breakdown of catecholamines. Low levels of SAMe combined with high levels of SAH will decrease COMT activity. As dopamine breakdown occurs at a normal rate, it may be advisable to monitor levels if VDR activity is low.			
VDR	rs731236	CC	●●
Your VDR genotype is associated with impaired metabolism, transport and storage of vitamin D and so an increased risk of deficiency. This can decrease serotonin and dopamine synthesis, leading to an increased need for dopamine precursors and methyl donors. This effect is exacerbated by high COMT activity, as dopamine is broken down more quickly. Lower COMT activity, and therefore slower dopamine breakdown, may result in normal levels.			
MAOA	rs6323	GG	-
You carry the "normal" genotype, which is associated with high MAOA enzyme activity and rapid breakdown of neurotransmitters leading to lower levels of neurotransmitters in the brain. This can lead to low mood and is linked with inward anger, depression, risk aversion and sleep disturbances. Females with this genotype who have experienced childhood trauma are more likely to exhibit aggression and experience sad moods.			
MAOB	rs1799836	AA	-
You carry alleles associated with normal MAOB enzyme activity, leading to efficient breakdown of neurotransmitters and some pharmaceuticals with a reduced susceptibility to negative moods.			

Specific Gene Advice

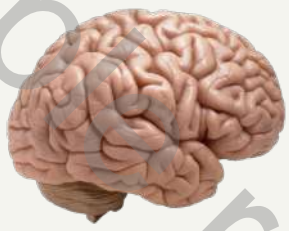
Based on specific gene results we also have the following recommendations:

Gene	Recommendation
MTHFR (A1298C)	You do not carry variants for this particular SNP, and so methylfolate is pulled into the BH4 cycle at a normal rate.
VDR (TaqI)	To ensure adequate vitamin D intake, incorporate foods like salmon, mackerel, egg yolks, dairy products, and mushrooms into your diet. To support methylfolate (5-MTHF) production, increase your intake of folate by consuming green leafy vegetables, bean and legumes, as well as cofactors vitamin B2 with foods like yogurt, almonds, and liver, and vitamin B3 with chicken, tuna, peanuts, and brown rice.
MAOA	If experiencing depression, anger and sleep disturbance, it may be helpful to increase your intake of curcumin (found in turmeric) and quercetin (colourful fruits and vegetables). These have been shown to moderate MAOA enzyme activity and may be beneficial for your genotype.

Advice for you

Here's some recommended lifestyle tips and practices based on your result

With these genetic results it is important to consider your intake of the B group vitamins and important cofactors such as vitamins D and C. SAMe levels are also important, if found to be low then supplementation may also be considered, as it is not possible to increase through dietary changes.



Doing a urine test to check neurotransmitter balances as well as a plasma SAH:SAMe ratio test may be considered.

Focus on eliminating heavy metals from your system, particularly mercury, lead, and aluminum. These toxic metals can accumulate in the body and disrupt biological processes. Mercury is found in fish like tuna, swordfish, and king mackerel. Lead exposure can come from old paints, contaminated water, and certain pottery and aluminum is often present in food additives, some cosmetics, and cookware.

Urea Cycle

Urea Cycle

Your Urea Cycle results show a Normal Efficiency

NORMAL | MODERATE | IMPAIRED

Detoxification | Cardiovascular function | Muscle function

Detailed Summary

The Urea cycle, or ornithine cycle, is a series of biochemical reactions that convert toxic ammonia into urea, which the kidneys can then excrete. This essential process occurs in the liver with the help of enzymes located in both the mitochondria and the cytosol of the cell.

First, ammonia (from The Transsulphuration Pathway) is converted into a compound that combines with ornithine to produce citrulline. Citrulline then moves from the mitochondria to the cytosol, where it combines with aspartate to form arginosuccinate. Arginosuccinate breaks down into arginine and fumarate. Fumarate enters another cycle to become aspartate again while arginine is broken down into urea and ornithine. Ornithine returns to the mitochondria to restart the cycle. Urea is the only new product, while all other molecules are recycled.

Nitric oxide (NO) is a crucial mediator that protects against atherosclerosis and helps regulate vasodilation. It is produced from arginine with the co-factor tetrahydrobiopterin (BH4) from The BH4 Cycle. Adequate levels of BH4 are essential for the proper functioning of nitric oxide synthase (NOS). Without sufficient BH4, NOS produces harmful free radicals such as peroxynitrite and superoxide instead of nitric oxide, leading to compromised cardiovascular function and increased risk of vascular diseases.

Considerations

When investigating the efficiency of the urea cycle, doing a Blood Urea Nitrogen (BUN) test to check your kidneys' efficiency at excreting urea, as well as a blood test to assess ammonia levels, could be beneficial.

Key Genes

NOS3 - this gene provides instructions for making the endothelial form of nitric oxide synthase which, along with other enzymes, produces nitric oxide in a process that relies on BH4 as a necessary cofactor. Endothelial NOS mainly makes nitric oxide (NO) in the lining of blood vessels. It is important because it helps widen blood vessels, which regulates blood flow and pressure. It also affects other processes like cell growth, the stickiness of white blood cells to blood vessel walls, and the clumping together of platelets in blood clotting. This function is vital for cardiovascular health, aiding in blood pressure regulation and the transportation of oxygen and nutrients throughout the body.

SOD2 - SOD (superoxide dismutase) enzymes form a group that catalyses the conversion of superoxide into oxygen and hydrogen peroxide, safeguarding cells against the damaging effects of superoxide.

Your Genetic Results

The below table shows the genes analysed in relation to your Urea Cycle Efficiency. For each gene you will see its name, location (RSID), your genotype, effect, and further information on your variants.

Gene	Location	Genotype	Effect
NOS3	rs1799983	GG	-
Your genotype is associated with normal NOS3 activity and a healthy production of nitric oxide. However, insufficient BH4 levels and excess ammonia can adversely impact NOS3 activity across all genotypes.			
SOD2	rs4880	CC	-
Your genotype indicates normal SOD2 enzyme activity, which effectively neutralises superoxide. However, low manganese levels can reduce SOD2 activity regardless of your genotype.			

Specific Gene Advice

Based on specific gene results we also have the following recommendations:

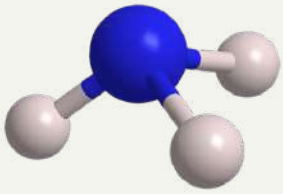
Gene	Recommendation
SOD2	This genotype results in normal enzyme activity, however you can support SOD by ensuring adequate intake of manganese. Good sources include brown rice, spinach, pineapple and whole wheat bread. Consume antioxidant-rich foods such as berries, colourful vegetables and spices such as ginger and tumeric to reduce oxidative stress.

Advice for you

Here's some recommended lifestyle tips and practices based on your result

Although genetically your Urea Cycle is efficient, it is still important to ensure sufficient intake of manganese to support SOD activity as well as vitamins B9, B2 and B3 to support 5-MTHF production and maintain sufficient levels of BH4. Including antioxidant-rich sources will be beneficial to protect the body from oxidative stress and free radical damage.

Green leafy vegetables, fatty fish and animal proteins and by-products such as eggs, and milk are excellent sources of B vitamins. Manganese can be found in foods like chickpeas, lentils, hazelnuts and pecans. Antioxidant-rich foods include berries, dark chocolate, nuts, herbs and spices, and citrus fruits.



Despite your genetic results, other factors can still affect this cycle. It may be of interest to do a Blood Urea Nitrogen (BUN) test to check your kidneys' efficiency at excreting urea, as well as a blood test to assess ammonia levels - excessive ammonia can inhibit nitric oxide production leading to issues with blood vessel dilation and inflammation, increasing heart risks in people with autoimmune diseases. In chronic kidney disease, high ammonia can worsen vasodilation, raise blood pressure, and accelerate atherosclerosis, especially in diabetic patients.