METHYLATION DEMO

Name: METHYLATION DEMO Date of Birth: 01-01-1111

Gender: Male Age: 01 Height:

Weight:

Fasting: NOT FASTING

Telephone: 000-000-0000

Street Address:

Email:

FINAL REPORT

Accession ID: 2312146745

Practice Name: DEMO CLIENT, MD

Provider Name: DEMO CLIENT, MD

Phlebotomist: 0

Telephone: 000-000-0000 Address: 3521 Leonard Ct, Santa

Clara, CA 95054

Report Information

Provider Information

Current Result Previous Result

In Control Moderate Risk

Specimen Information

Sample Type	Collection Time	Received Time	Report	Final Report Date
Serum	2023-12-22 13:00 (PDT)	2023-12-27 10:45 (PDT)	Methylation - P2	2024-01-01 16:33 (PDT)
EDTA	2023-12-22 13:00 (PDT)	2023-12-27 10:45 (PDT)	Methylation - P2	2024-01-01 16:33 (PDT)





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INTRODUCTION

Vibrant Wellness is pleased to present to you, 'Methylation Panel', to help you make healthy lifestyle, dietary and treatment choices in consultation with your healthcare provider. It is intended to be used as a tool to encourage a general state of health and well-being. The Vibrant Methylation Panel is a test to measure levels of various genetic mutations present in an individual's body which could affect methylation pathways. The panel is designed to give a complete picture of these predispositions along with the actual measure of the homocysteine, Vitamin B9(Folate) and Vitamin B12.

Methodology:

The Vibrant Methylation Genetics panel uses real-time PCR methodology. DNA is extracted and purified from blood samples and a SNP (single nucleotide polymorphism) genotyping assay is performed using real-time PCR to detect the specific allele targets of each assay performed.

Interpretation of Report:

The genetic mutations on the report are organized as multiple tables under different subheadings for associated markers. The mutation alleles are indicated with a + symbol and wild type alleles are indicated with a - symbol. Risk associated variants are indicated with red and alleles with no risk are indicated with green. All contents provided in the report are purely for informational purposes only and should not be considered medical advice. Any changes based on the information provided should be made in consultation with the clinical provider.

The Vibrant Wellness platform provides tools for you to track and analyze your general wellness profile. Testing for the Methylation Genetics panel is performed by Vibrant Genomics, a CLIA certified lab CLIA#: 05D2098445. Vibrant Wellness provides and makes available this report and any related services pursuant to the Terms of Use Agreement (the "Terms") on its website at www.vibrant-wellness.com. By accessing, browsing, or otherwise using the report or website or any services, you acknowledge that you have read, understood, and agree to be bound by these terms. If you do not agree to these terms, you shall not access, browse, or use the report or website. The statements in this report have not been evaluated by the Food and Drug Administration and are only meant to be lifestyle choices for potential risk mitigation. Please consult your physician for medication, treatment, diet, exercise, or lifestyle management as appropriate. This product is not intended to diagnose, treat, or cure any disease or condition.

Please note:

It is important that you discuss any modifications to your diet, exercise, and nutritional supplementation with your physician before making any changes. The Vibrant America Clinical Support team can only provide basic and generalized interpretation of hormone biomarkers and pathways.





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Methylation - Summary

Methylation ⊕ ⊕ Homozygous Mutant → Heterozygous Homozygous Wild **Test Name** Gene Name **Risk Association Your Mutation** Your Risk Reference Methionine and SAMe build up in $\oplus \oplus \top / \top$ rs10948059 **GNMT** Elevated C/C the blood

The glycine N-methyltransferase gene (GNMT) regulates the production of the enzyme glycine N-methyltransferase which is involved in the methylation of glycine and S-adenosylmethionine (SAMe) to N-dimethylglycine and S-adenosylhomocysteine (SAH) involved in cell growth and the regulation of gene expression. The mutation causes decreased expression of the gene and impairs the breakdown of methionine and SAMe, causing it to build up in the blood, abnormal methylation of DNA, cytotoxicity, and impaired DNA formation. Homozygous mutant (abnormal) individuals may have decreased gene expression and impaired methylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like magnesium and folate can also be beneficial.

rs3733890

BHMT

Homocysteine builds up in the bloodstream



Elevated

G/G

BHMT gene encodes the betaine-homocysteine S-methyltransferase enzyme that catalyzes the remethylation of homocysteine (Hcy) to methionine with betaine as the methyl donor. Methionine is then converted to SAM, the key methyl donor required for histone and DNA methylation. SAMe plays a role in the immune system, maintains cell membranes, and helps produce and break down brain chemicals, such as serotonin, melatonin, and dopamine. The mutation disrupts gene activity and prevents the enzyme from functioning normally. Without methionine synthase reductase, methionine synthase cannot convert homocysteine to methionine leading to impaired methylation. As a result, homocysteine builds up in the bloodstream, which is associated with the risk of developing dementia, heart disease, and stroke. Homozygous mutant (abnormal) individuals who have disrupted gene activity have impaired methylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like magnesium, zinc, betaine, or choline supplementation and folate can also be beneficial.

rs1801133

MTHFR

Active folate deficiency



Partially elevated

C/C

The MTHFR gene encodes for the methylenetetrahydrofolate reductase enzyme. The enzyme catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, an active form of folate. Folate is a methyl donor that plays an essential role in DNA synthesis and biological methylation reactions, including DNA methylation. Folate deficiency may be implicated in the development of genomic DNA hypomethylation, which is an early epigenetic event found in many cancers, particularly colorectal cancer (CRC). A mutation in the gene leads to MTHFR gene deficiency affecting the gene activity to form active folate. Thus, the mutations lead to impaired DNA methylation associated with the risk of developing neural tube defects. Heterozygous (partially abnormal) individuals who have gene deficiency are associated with impaired methylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like magnesium and folate can also be beneficial.

rs1801394

MTRR

Failure to convert homocysteine to methionine



Partially elevated

A/A

The MTRR gene provides instructions for making an enzyme called methionine synthase reductase. This enzyme is required for the proper function of another enzyme called methionine synthase. Methionine synthase catalyzes the remethylation of homocysteine to regenerate methionine and generate S-adenosylmethionine, the most important cellular methyl donor. SAMe plays a role in the immune system, maintains cell membranes, and helps produce and break down brain chemicals, such as serotonin, melatonin, and dopamine. The mutation disrupts gene activity and prevents the enzyme from functioning normally. Without methionine synthase reductase, methionine synthase cannot convert homocysteine to methionine leading to impaired methylation. As a result, homocysteine builds up in the bloodstream, which is associated with the risk of developing dementia, heart disease, and stroke. Heterozygous (partially abnormal) individuals who have disrupted gene activity have impaired methylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like Vitamin B12, and folate can also be beneficial.



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Methylation - Summary

A/A

Methylation	1	⊕ ⊕ Hom	ozygous Mutant	⊕ ⊖ Heterozygous	→ Homozygous Wild
Test Name	Gene Name	Risk Association	Your Mutation	Your Risk	Reference
rs1979277	SHMT1	Active folate deficiency	⊕⊝C/T	- Partially elevate	d C/C

The SHMT1 gene encodes the production of the enzyme serine hydroxymethyltransferase 1. This enzyme catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, an active form of folate. Folate is a methyl donor that plays an essential role in DNA synthesis and biological methylation reactions, including DNA methylation. A mutation in the gene leads to gene deficiency affecting the gene activity to form active folate. Thus, the mutations lead to impaired DNA methylation associated with the risk of developing neural tube defectsHeterozygous (partially abnormal) individuals who have gene deficiency activity have impaired methylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like Vitamin B6, SAMe, and folate can also be beneficial.

rs162036 MTRR Homocysteine builds up in the bloodstream + - A/G Partially elevated

The MTRR gene provides instructions for making an enzyme called methionine synthase reductase. This enzyme is required for the proper function of another enzyme called methionine synthase. Methionine synthase catalyzes the remethylation of homocysteine to regenerate methionine and generate S-adenosylmethionine, the most important cellular methyl donor. SAMe plays a role in the immune system, maintains cell membranes, and helps produce and break down brain chemicals, such as serotonin, melatonin, and dopamine. The mutation in disrupts gene activity and prevents the enzyme from functioning normally. Without methionine synthase reductase, methionine synthase cannot convert homocysteine to methionine leading to impaired methylation. As a result, homocysteine builds up in the bloodstream, which is associated with the risk of developing dementia, heart disease, and stroke. Heterozygous (partially abnormal) individuals who have disrupted gene activity have impaired methylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like magnesium and folate can also be beneficial.

rs1805087 MTR Active folate deficiency $+ \bigcirc A/G$ Partially elevated A/A

The MTR gene encodes an enzyme called methionine synthase. Methionine synthase catalyzes the remethylation of homocysteine to regenerate methionine and generate S-adenosylmethionine, the most important cellular methyl donor. SAMe plays a role in the immune system, maintains cell membranes, and helps produce and break down brain chemicals, such as serotonin, melatonin, and dopamine. The mutation disrupts gene activity and prevents the enzyme from functioning normally. Without methionine synthase reductase, methionine synthase cannot convert homocysteine to methionine leading to impaired methylation. As a result, homocysteine builds up in the bloodstream, which is associated with the risk of developing dementia, heart disease, and stroke. Heterozygous (partially abnormal) individuals who have disrupted gene activity have impaired methylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like magnesium and folate can also be beneficial.

rs4680 COMT Abnormal catechol-0-methyltransferase levels + A/G Partially elevated G/G

The COMT gene encodes the catechol-O-methyltransferase enzyme which transfers methyl groups (hence the name methyltransferase). COMT introduces a methyl group to the catecholamine (dopamine, epinephrine, and norepinephrine). The mutation in the gene leads to the loss of one copy of the COMT gene in each cell leading to abnormal regulation of catechol-O-methyltransferase levels in the brain. This leads to undermethylation(refers to a low catecholamine level) and may not produce enough key neurotransmitters for mental health, which may be associated with the risks of developing depression and other mental health symptoms. Heterozygous (partially abnormal) individuals who have a loss of one copy of the COMT gene show undermethylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like magnesium and folate can also be beneficial.



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Methylation - Summary

Methylation	1	⊕ ⊕ Hon	nozygous Mutant	⊕ Heterozygous	● ● Homozygous Wild
Test Name	Gene Name	Risk Association	Your Mutatio	n Your Risk	Reference
rs4633	COMT	Abnormal catechol-O- methyltransferase levels	⊕⊝C/ ⁻	Partially elevate	ed C/C

The COMT gene encodes the catechol-O-methyltransferase enzyme which transfers methyl groups (hence the name methyltransferase). COMT introduces a methyl group to the catecholamine (dopamine, epinephrine, and norepinephrine). The mutation in the gene leads to the loss of one copy of the COMT gene in each cell leading to abnormal regulation of catechol-O-methyltransferase levels in the brain. This leads to undermethylation(refers to a low catecholamine level) and may not produce enough key neurotransmitters for mental health, which may be associated with the risks of developing depression and other mental health symptoms. Heterozygous (partially abnormal) individuals who have a loss of one copy of the COMT gene show undermethylation. Individuals with genetic susceptibility may benefit from consuming methylated folate supplements. Foods like kale, spinach, bok choy, escarole, collard greens, beet greens, mustard greens, turnip greens, arugula, broccoli, cabbage, Brussels sprouts, cauliflower, beetroot, beans, legumes, okra, mushroom, beef liver, the chicken liver can be included in the diet. Dietary supplements like magnesium and folate can also be beneficial.

Serum Markers					
Test Name	Current	Previous		Result	Reference
Vitamin B12 Serum (pg/mL)	1317		0 231	1245	232.0-1245.0

The nutrient, vitamin B12 is required for the action of methionine synthase in the remethylation process. In this process, methionine synthase converts homocysteine to methionine. A vitamin B12 deficiency can lead to the blocking of the methylation pathway which may cause the folate cofactors in the cell to become trapped as 5-methyltetrahydrofolate (a form of folate). This process in turn produces a pseudo folate deficiency in cells, which could prevent cell division and give rise to anaemia, identical to that seen in folate deficiency.



Homocysteine (Hcy) is a naturally occurring amino acid produced during the methylation process. The concentrations of Hcy are maintained by two routes; particularly, the remethylation pathway, where Hcy is converted back to methionine, and the transsulfuration pathway, where Hcy is converted to cystathionine to form cysteine. Thus, altered gene activity in any of the given pathways can affect these processes resulting in altered levels of Hcy in blood. Elevated plasma Hcy is a risk factor for cardiovascular disease and Alzheimer's disease. Additionally, the reactions that remove Hcy are very sensitive to B vitamin status, including B12, B6 and folate, as these vitamins are required for the breakdown of Hcy. As a result, elevated Hcy levels can also be indicative of a deficiency in the above-mentioned nutrients.



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Methylation

TVICE Date. 202	3-12-27 10:45 (PDT	,			
Methylation	1	⊕ ⊕ Homoz	zygous Mutant	→ Heterozygous	
Test Name	Gene Name	Risk Association	Your Mutatio	n Your Risk	Reference
rs1801133	MTHFR	Active folate deficiency	⊕ ⊝C/¯	Partially elevate	ed C/C
rs1801131	MTHFR	Active folate deficiency	(+)(+)(+)	Normal	A/C, A/A
rs1801394	MTRR	Failure to convert homocysteine to methionine	⊕ ⊝A/(Partially elevate	ed A/A
rs3851059	MAT1A	Homocysteine builds up in the bloodstream	+++G/(Normal	G/G
rs1979277	SHMT1	Active folate deficiency	⊕⊝C/¯	Partially elevate	ed C/C
rs10948059	GNMT	Methionine and SAMe build up in the blood	(+)	Elevated	C/C
rs3733890	ВНМТ	Homocysteine builds up in the bloodstream	$\bigcirc\bigcirc$ A/A	Elevated	G/G
rs162036	MTRR	Homocysteine builds up in the bloodstream	⊕ ⊝A/0	Partially elevate	ed A/A
rs1805087	MTR	Active folate deficiency	⊕ ⊝A/0	Partially elevate	ed A/A
rs4680	СОМТ	Abnormal catechol-O- methyltransferase levels	⊕⊝A/(Partially elevate	ed G/G
rs4633	сомт	Abnormal catechol-O- methyltransferase levels	⊕⊝C/	Partially elevate	ed C/C
rs1799983	NOS3	Reduced NO levels	99G/0	Normal	G/G
Serum Mar	kers				
Test Name		Current Previous		Result	Reference
Homocysteine	(μmol/L)	10	0 9	14	≤9.0
Vitamin B12 Se	erum (pg/mL)	1317	0 231	1245	232.0-124
Folate Serum (ng/mL)	>20	0	4.5	≥4.6



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Methylation

Risk and Limitations

This test has been developed and its performance characteristics determined and validated by Vibrant Genomics LLC., a CLIA certified lab. These assays have not been cleared or approved by the U.S. Food and Drug Administration. Vibrant Wellness provides additional contextual information on these tests and provides the report in a more descriptive fashion.

The Vibrant CardiaX Genetics panel does not demonstrate absolute positive and negative predictive values for any condition. Its clinical utility has not been fully established. Clinical history and current symptoms of the individual must be considered by the healthcare provider prior to any interventions. Test results should be used as one component of a physician's clinical assessment.

CardiaX Genetics testing is performed at Vibrant Genomics, a CLIA certified laboratory. Vibrant Genomics has effective procedures in place to protect against technical and operational problems. However, such problems may still occur. Examples include failure to obtain the result for a specific test due to circumstances beyond Vibrant's control. Vibrant may re-test a sample to obtain these results but upon re-testing the results may still not be obtained. As with all medical laboratory testing, there is a small chance that the laboratory could report incorrect results. A tested individual may wish to pursue further testing to verify any results.

Genetic testing is helpful in analyzing the risk of various diseases. However, it is important to note that Genetic risk determinants are neither necessary nor sufficient for the development of diseases. Environmental and lifestyle risk factors could also affect the risk of disease development. Results from genetic analysis should always be interpreted along with clinical findings on the individual. Genetic testing evaluates only for the genotypes indicated; it does not test for other genetic abnormalities found elsewhere in the genome. Different genetic variants can be tested by different genetic labs to evaluate the risk for a particular disease, depending on what is tested, genetic risk may not be comparable between labs. It should be realized that there are possible sources of error like any lab testing which include sample misidentification, trace contamination of PCR reactions, technical errors and rare genetic variants that may interfere with analysis.

Some individuals may feel anxious about getting their genetic test health results. If the potential user feels very anxious, such user should speak to his or her doctor or other health care professional prior to collection of a sample for testing. Users should consult with their doctor or other health care professional if they have any questions or concerns about the results of their test or their current state of health. Users of the test are also encouraged to discuss their test results with a genetic counselor, board-certified clinical molecular geneticist, or equivalent health care professional.

The information in this report is intended for educational purposes only. While every attempt has been made to provide current and accurate information, neither the author nor the publisher can be held accountable for any errors or omissions. Tested individuals may find their experience is not consistent with Vibrant's selected peer reviewed scientific research findings of relative improvement for study groups. The science in this area is still developing and many personal health factors affect diet and health. Since subjects in the scientific studies referenced in this report may have had personal health and other factors different from those of tested individuals, results from these studies may not be representative of the results experienced by tested individuals. Further, some recommendations may or may not be attainable, depending on the tested individual's physical ability or other personal health factors. A limitation of this testing is that many of these scientific studies may have been performed in selected populations only. The interpretations and recommendations are done in the context of these studies, but the results may or may not be relevant to tested individuals of different or mixed ethnicities.

Vibrant Wellness makes no claims as to the diagnostic or therapeutic use of its tests or other informational materials. Vibrant Wellness reports and other information do not constitute medical advice and are not a substitute for professional medical advice. Please consult your healthcare practitioner for questions regarding test results, or before beginning any course of medication, supplementation, or dietary changes.



