DEMO DEMO

Name: DEMO DEMO Date of Birth: 10-29-1971 Biological Sex: Male

Age: 54 Height: Weight:

Telephone: 000-000-0000

Street Address:

Email:

FINAL REPORT

Accession ID: 2738942934

Fasting: NOT FASTING

Practice Name: DEMO CLIENT, MD

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

Clara, CA 95054

Provider Information

Provider Name: DEMO CLIENT, MD Phlebotomist: 0

Report 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 21:00 (UTC)	2023-12-27 18:45 (UTC)	Methylation - P2	2024-01-02 00:33 (UTC)
EDTA	2023-12-22 21:00 (UTC)	2023-12-27 18:45 (UTC)	Methylation - P2	2024-01-02 00:33 (UTC)



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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 variants 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 variants on the report are organized as multiple tables under different subheadings for associated markers. The summary page lists the set of analytes with risk associated variants. Following this section is the complete list of the genetic markers measured in the panel. Elevated risk associated variants are indicated with red, partially elevated risk associated variants are indicated with yellow 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. By accessing or using this report, you acknowledge that you have read and understood the Risks and Limitations – Genetics section and agree to consider its contents when interpreting your results. 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 healthcare provider 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 healthcare provider before making any changes.



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Methylation + Homozygous Mutant → Heterozygous Homozygous Wild Test Name Gene Name **Risk Association** Your Mutation Your Risk Reference Failure to convert homocysteine to +-A/G rs1801394 **MTRR** A/A Elevated methionine

The MTRR gene provides instructions for producing the enzyme methionine synthase reductase, which is essential for the proper function of methionine synthase. Methionine synthase catalyzes the remethylation of homocysteine to regenerate methionine and produce S-adenosylmethionine (SAMe), a key cellular methyl donor. SAMe supports the immune system, maintains cell membranes, and is involved in the synthesis and breakdown of brain chemicals such as serotonin, melatonin, and dopamine. Mutations in the MTRR gene can disrupt enzyme activity, preventing methionine synthase from efficiently converting homocysteine to methionine. This leads to impaired methylation and accumulation of homocysteine in the bloodstream, which is associated with an increased risk of dementia, cardiovascular disease, and stroke.Individuals with GG genotype with 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.

rs1979277 SHMT1 Active folate deficiency + - C/T Elevated C/C

The SHMT1 gene encodes the enzyme serine hydroxymethyltransferase 1, which catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, an active form of folate. Folate serves as a critical methyl donor essential for DNA synthesis and biological methylation reactions, including DNA methylation. Mutations in the SHMT1 gene can impair the production of active folate, leading to disrupted DNA methylation and an increased risk of developing neural tube defects. Individuals with TT genotype have impaired gene activity 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 Vitamin B6, SAMe, and folate can also be beneficial.

The glycine N-methyltransferase (GNMT) gene regulates the production of the enzyme glycine N-methyltransferase, which catalyzes the methylation of glycine using S-adenosylmethionine (SAMe) to produce N-dimethylglycine and S-adenosylhomocysteine (SAH). This process is essential for cell growth and the regulation of gene expression. Mutations in the GNMT gene can decrease its expression, impairing the breakdown of methionine and SAMe. This leads to their accumulation in the blood, abnormal DNA methylation, cytotoxicity, and disrupted DNA synthesis. Individuals with TT genotype 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 Homocysteine builds up in the

The BHMT gene encodes the enzyme betaine-homocysteine S-methyltransferase, which catalyzes the remethylation of homocysteine (Hcy) to methionine using betaine as the methyl donor. Methionine is then converted to S-adenosylmethionine (SAMe), a key methyl donor required for DNA and histone methylation. SAMe also supports the immune system, maintains cell membranes, and aids in the synthesis and breakdown of brain chemicals, including serotonin, melatonin, and dopamine. Mutations in the BHMT gene disrupt enzyme activity, impairing the conversion of homocysteine to methionine. This leads to elevated homocysteine levels in the bloodstream and impaired methylation, increasing the risk of dementia, heart disease, and stroke.Individuals with AA genotype 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.



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Methylation		⊕ ⊕ Homozyg	jous Mutant ⊕ ⊖ Hete	erozygous \varTheta 👄 Ho	omozygous Wild
Test Name	Gene Name	Risk Association	Your Mutation	Your Risk	Reference
rs1801133	MTHFR	Active folate deficiency	⊕⊝C/T	Partially elevated	C/C

The MTHFR gene encodes the enzyme methylenetetrahydrofolate reductase, which catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, an active form of folate. Folate serves as a methyl donor essential for DNA synthesis and methylation reactions, including DNA methylation. Folate deficiency can contribute to genomic DNA hypomethylation, an early epigenetic event observed in many cancers, particularly colorectal cancer (CRC). Mutations in MTHFR impair the production of active folate, leading to defective DNA methylation and an increased risk of developing neural tube defects. Individuals with CT genotype who have impaired gene activity 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.

rs162036 MTRR Homocysteine builds up in the homocysteine bloodstream Homocysteine bloodstream

The MTRR gene provides instructions for producing the enzyme methionine synthase reductase, which is essential for the proper function of methionine synthase. Methionine synthase catalyzes the remethylation of homocysteine to regenerate methionine and produce S-adenosylmethionine (SAMe), a crucial cellular methyl donor. SAMe supports the immune system, maintains cell membranes, and is involved in the synthesis and breakdown of brain chemicals such as serotonin, melatonin, and dopamine. Mutations in the MTRR gene disrupt enzyme activity, impairing methionine synthase function. This leads to reduced conversion of homocysteine to methionine, impaired methylation, and elevated homocysteine levels in the bloodstream, increasing the risk of dementia, heart disease, and stroke.Individuals with AG genotype 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 Homocysteine builds up in the bloodstream + A/A Partially elevated A/A

The MTR gene encodes the enzyme methionine synthase, which catalyzes the remethylation of homocysteine to regenerate methionine and produce S-adenosylmethionine (SAMe), a key cellular methyl donor. SAMe is essential for immune function, maintaining cell membranes, and the synthesis and breakdown of brain chemicals such as serotonin, melatonin, and dopamine. Mutations in the MTR gene disrupt enzyme activity, impairing the conversion of homocysteine to methionine and leading to defective methylation. Consequently, homocysteine accumulates in the bloodstream, increasing the risk of dementia, heart disease, and stroke.Individuals with AG genotype 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-0methyltransferase levels + A/G Partially elevated G/G

The COMT gene encodes the enzyme catechol-O-methyltransferase, which transfers methyl groups to catecholamines, including dopamine, epinephrine, and norepinephrine. Mutations in the gene can result in the loss of one copy of COMT in each cell, leading to abnormal regulation of enzyme levels in the brain. This can cause undermethylation, reflected by reduced catecholamine activity, potentially impairing the production of key neurotransmitters essential for mental health. Such alterations may increase the risk of developing depression and other mental health-related symptoms. Individuals with AG genotype 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		⊕ ⊕ Homozyg	ous Mutant (Ð ⊖ Heterozygous	● ● Homozygous Wild
Test Name	Gene Name	Risk Association	Your Muta	ation Your	Risk Reference
rs4633	COMT	Abnormal catechol-O- methyltransferase levels	+ -C	;/T Partially 6	elevated C/C

The COMT gene encodes the catechol-O-methyltransferase enzyme, which transfers methyl groups to catecholamines such as dopamine, epinephrine, and norepinephrine. Mutations in the gene can lead to the loss of one copy of COMT in each cell, resulting in abnormal regulation of enzyme levels in the brain. This can cause undermethylation—characterized by reduced catecholamine activity—and may impair the production of key neurotransmitters, potentially increasing the risk of depression and other mental health disorders.Individuals with CT genotype 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

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Methylation		⊕ ⊕ Homozyg	ous Mutant	⊕ ⊕ Het	erozygous 🕒 👄 I	Homozygous Wild
Test Name	Gene Name	Risk Association	Your M	utation	Your Risk	Reference
rs1801133	MTHFR	Active folate deficiency	••	C/T	Partially elevated	I C/C
rs1801131	MTHFR	Active folate deficiency	$\bigcirc\bigcirc$	A/A	Normal	A/A
rs1801394	MTRR	Failure to convert homocysteine to methionine	· +-	A/G	Elevated	A/A
rs3851059	MAT1A	Homocysteine builds up in the bloodstream	$\bigcirc\bigcirc$	G/G	Normal	G/G
rs1979277	SHMT1	Active folate deficiency	$\oplus \ominus$	C/T	Elevated	C/C
rs10948059	GNMT	Methionine and SAMe build up in the blood	(+) (+)	T/T	Elevated	C/C
rs3733890	ВНМТ	Homocysteine builds up in the bloodstream	++	A/A	Elevated	G/G
rs162036	MTRR	Homocysteine builds up in the bloodstream	+ -	A/G	Partially elevated	I A/A
rs1805087	MTR	Homocysteine builds up in the bloodstream	$\oplus \ominus$	A/G	Partially elevated	I A/A
rs4680	сомт	Abnormal c <mark>atecho</mark> l-O- methyltransf <mark>erase leve</mark> ls	$\oplus \ominus$	A/G	Partially elevated	I G/G
rs4633	сомт	Abnormal ca <mark>techol-O-</mark> methyltransfera <mark>se le</mark> vels	(+) (-)	C/T	Partially elevated	I C/C
rs1799983	NOS3	Altered DNA Methylation	$\Theta\Theta$	G/G	Normal	G/G
Serum Marker	s					
Test Name		Current Previous		Resul	t	Reference
Homocysteine (µm	ol/L)	10	9	14		≤9.0
Vitamin B12 Serum	ı (pg/mL)	1317	231		1245	232.0-1245.
Folate Ser <mark>um (</mark> ng/m	nL)	>20		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 Methylation 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 healthcare provider's clinical assessment.

Methylation panel 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.

The supplement recommendations and dosage guidelines provided are intended for general informational purposes only and should not replace professional medical advice; final dosage decisions must be made in consultation with your healthcare provider. Vibrant disclaims any liability for adverse effects, outcomes, or consequences arising from the use of these suggestions.



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Methylation

Risks and Limitations - Genetics

Genetic testing is helpful in analyzing risks to various diseases. However, it is essential 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. 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 the analysis.

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.

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 collecting 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.

Variant risk classification may not align with associated disease risk or may change ex: a benign variant may be reported as pathogenic. Misclassification may be due to updated research studies, allele dropouts or interpretation pitfalls. Variant risk classification may also not be relevant to the tested individual of different or mixed ethnicities in comparison to the study group(s) from literature. Vibrant conducts internal audits, post market surveillance and feedback from providers and customers on an ongoing basis to keep our reports updated with the most current findings. 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 prior to any interventions and diet/supplement/lifestyle changes.

Genetic SNP testing is performed using real time PCR systems. It is important to note that allele calling for a particular SNP is performed using the Autocall methodology of the instrument manufacturer. Failure or error in autocalling could occur and is usually associated with outlier wells or software issues relevant to making an allele call. As with all genetic SNP testing, there is a small chance that the laboratory could report these incorrect results.

Genetic testing is not intended to diagnose a disease, tell you anything about your current state of health, or be used to make medical decisions, including whether you should take a medication/supplement or how much of a medication/supplement you should take. It is intended to provide users with their genetic information and suggestions to inform lifestyle decisions and conversations with their doctor or other health care professionals.



