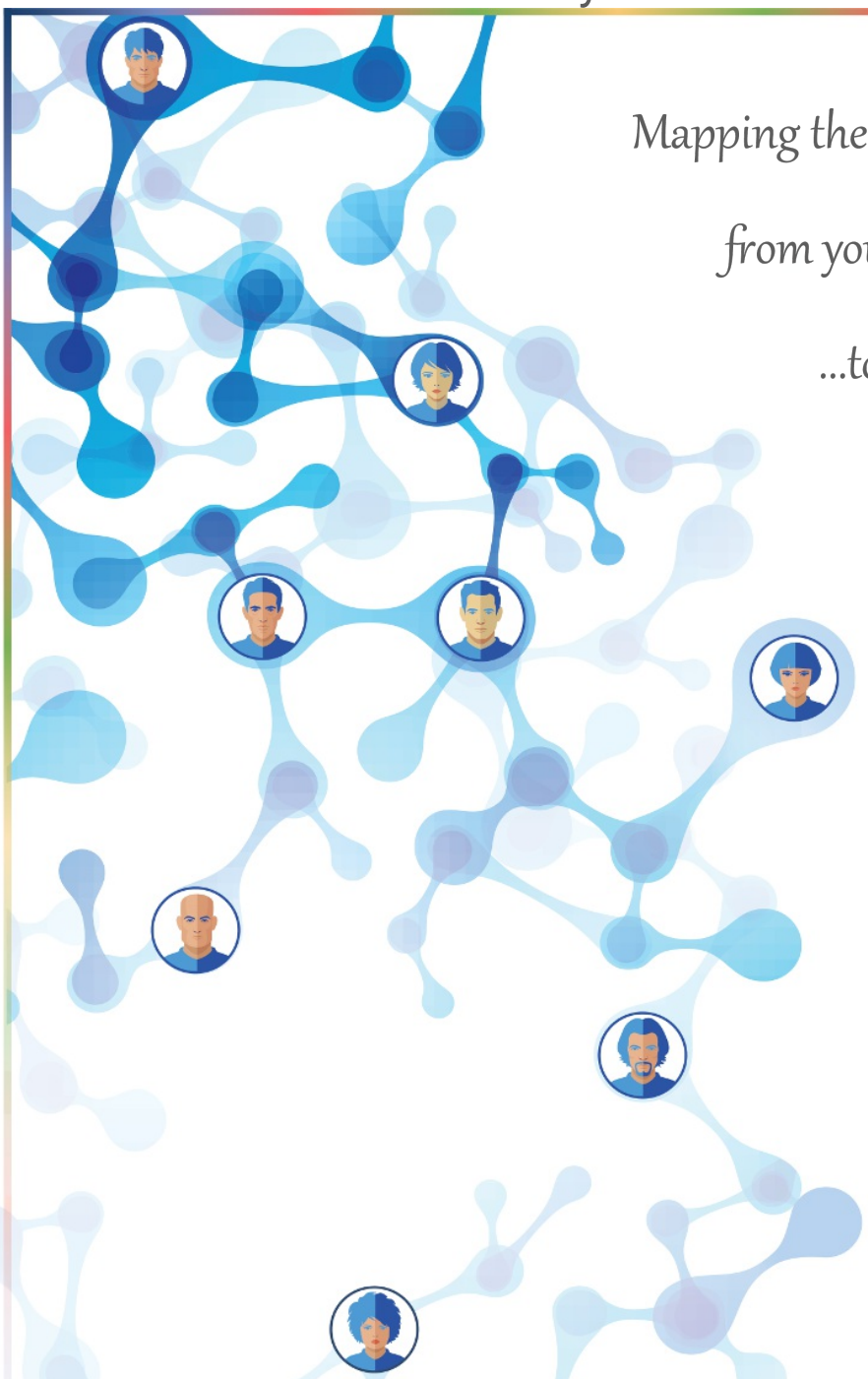
Defy Your DNA Program Report



Mapping the path

from your past...

...to your future

KASHI CLINICAL LABORATORIES

Delivering More Than A Test Result

This test detects only specific targeted genetic variations and there is a possibility that other genetic variants not detected by this test may be present. The DNA variants tested for in this report have been scientifically determined to be possible risk factors for the reported condition. The content of this report is provided for informational purposes only, not as a diagnostic tool. The report does not supersede the judgment of a qualified medical provider. This test is not a substitute for a comprehensive consideration of all factors that influence the maintenance of a healthy body. Genetic risk factors are not guarantees that you will develop a condition, and in many cases, the presence of a particular DNA variant may only play a minor role in your risk for disease, compared with environmental and lifestyle factors. This test is not FDA approved. The test's performance characteristics have been established and maintained by Kashi Clinical Laboratories under CLIA and CAP compliance.

Reported and Reviewed By:

Zahra Mehdizadeh Kashi, Ph.D., HCLD
CEO and Laboratory Director

PATIENT
PFirst PLast
DOB: 01/01/72

ORDERING PROVIDER
Example Organization

LABORATORY INFORMATION
Lab ID: 100000000HLA
Collection Date: 01/11/10
Test Date: 01/21/10
Report Date: 01/22/10

	GENE MARKER	RESULT	RISK	PARTIAL RISK	NON RISK	ASSOCIATION
WEIGHT	FTO	A/T		◐		Appetite regulation and craving frequency
	MC4R	C/T		◐		Satiety and metabolism regulation
	FABP2	G/G			❍	Dietary fat sources and fat utilization
	ADRB2	C/C			❍	Carbohydrate digestion and physical activity
	SH2B1	A/G		◐		Regulation of leptin and insulin
CARDIAC	9p21	G/G			❍	Plaque formation in coronary arteries
	NOS-D298E	G/T		◐		Blood pressure regulation and heart disease
	MTHFR-C677T	C/T			▼	Processing folate and regulating homocysteine
	MTHFR-A1298C	C/C			▼	Processing folate and regulating homocysteine
	AGT	T/T	●			Blood pressure regulation
	APOE*	E2/E3			❍	Fat and cholesterol transportation and levels
	SLCO1B1*5	C/C	●			Statin metabolism
NUTRITION	GC1/GC2*	TA/GA	●			Vitamin D binding & transport
	CYP2R1	G/A		◐		Vitamin D metabolism
	NADSYN1/DHCR7	T/G			❍	Vitamin D metabolism
	VDR-Bsm1	G/A		◐		Vitamin D and bone density
	VDR-Taq1	C/T		◐		Metabolic disease
	VDR-Fok1	C/T		◐		Endocrine function and cancer risk
	TMPRSS6	C/T		◐		Iron levels and iron deficiency
	BCMO1	T/G		◐		Conversion of beta carotene to vitamin A
	FUT2	A/G			❍	Vitamin B12, brain and nervous system function
GRACEFUL AGING	WNT16	C/T		◐		Bone mineral density
	ESR1-1	C/T		◐		Estrogen's impact on bone turnover
	ESR1-2	G/A			❍	Estrogen's impact on bone turnover
	COMT	VAL/MET			=	Catecholamine and estrogen metabolism
	CYP1A1	A/G		◐		Drug metabolism
	MAOA	C/T		◐		Regulation of neurotransmitters
	APOE*	E2/E3			❍	Plaque formation in brain tissue
METHYLATION	NOS-D298E	G/T		◐		Heart disease and cancer risk
	MTHFR-C677T	C/T			▼	Folate and Homocysteine levels
	MTHFR-A1298C	C/C			▼	Regulation of SAMe and folate levels
	CBS-A360A	C/T		◐		Homocysteine conversion to cystathionine & glutathione
	CBS-C699T	C/T		◐		Homocysteine conversion to cystathionine & glutathione
	MTR-A2756G	A/G		◐		Methionine and folate synthesis
	MTRR-A66G	A/G		◐		DNA methylation and cancer risk

GENOTYPE RISK KEY:
❍ Non Risk ◐ Partial Risk ● Risk ▲ Increased Enzyme Activity
▼ Decreased Enzyme Activity ▼ Decreased Enzyme Activity (no risk associated)
**Combined genotype, read section detail for further explanation.*

PATIENT: PFirst PLast LAB ID NUMBER: 100000000HLA

Important Information About Your Weight Management Test Results

FTO ◐

The FTO gene has been linked to obesity risk. This result is associated with weight gain around midsection, a greater increase in body mass, some increased risk of developing obesity in adulthood, cravings for calorie-dense and high-fat foods, and reduced feelings of fullness after meals.

MC4R ◐

The MC4R gene is associated with appetite control and weight gain. This result is associated with reduced sense of fullness after meals, increased craving for calorie dense and high fat foods, snacking behavior, and increased perception of hunger leading to weight gain. There can be increased risk for weight gain for sedentary individuals, and diminished insulin response in the brain.

FABP2 ○

The FABP2 protein helps in fat transportation and absorption. This result is associated with normal fat absorption and utilization.

ADRB2 ○

The ADRB2 gene is involved in carbohydrate digestion and weight loss with physical activity. This result is associated with normal response to exercise and is not associated with increased risk of high BMI.

SH2B1 ◐

The SH2B1 gene influences the balance of leptin and insulin in the blood. This result may be associated with increased feelings of hunger due to leptin resistance, overeating of calorie dense food groups, increased chance for insulin and leptin resistance, and weight gain from diets high in saturated fats. Eating larger than normal portions may occur.

TREATMENT CONSIDERATIONS

Eat five or more small meals a day which will help minimize hunger spikes, reduce inadvertent overeating, support an increased metabolism, and regulate insulin demand. Eat a higher amount of calories from protein which digests slowly, and a lower amount of calories from fat, thus encouraging use of existing fat stores. Eat foods that are low in calorie density like vegetables and fruits. Green leafy salads with a light dressing are a good choice, such that if portions are too large, the excess calories are from lower calorie-dense foods. Fatty foods have a higher calorie density and should be minimized. Choose complex carbohydrates like whole grains, low starch vegetables, and fruits with skin to increase fiber. This helps to control food cravings, blood sugar levels, leptin levels, insulin levels, and fat in the bloodstream. Eat 20-30 grams of protein with each meal to ensure slower digestion time, thus maintaining a consistent supply of proteins for healthy muscle tissue in order to support a healthy metabolism. Exercise to ensure muscle retention. Choose lean proteins like poultry and fish to reduce saturated fat intake. Ideally eat carbohydrates with a high fiber content that have a glycemic index of 55 or less.

ADDITIONAL COMMENTS

Practice mindful eating by chewing food slowly, allowing saliva to mix with the food to help prepare it for digestion. Chewing also helps stimulate release of enzymes that break down free fatty acids. Learn to manage stress because a strong relationship exists between obesity and elevated levels of the stress hormone cortisol. Meditation has been shown to modulate the stress hormones and neurotransmitters in the brain. With balanced levels of stress chemicals there may be less binge or emotional comfort eating. Green tea has been shown to influence the regulation of weight and can help with mood. Sleep at least 7-8 hours a night to rebuild and repair daily damage as well as to cement learning. The risk of obesity significantly increases at less than 6 hours sleep per night. Support detoxification with flavonoids.

PATIENT: PFirst PLast LAB ID NUMBER: 100000000HLA

Important Information About Your Cardiac Test Results

9p21 ❍	9p21 is associated with growth of arterial plaque. This result is not associated with increased risk of coronary artery disease or atherosclerosis.
NOS-D298E ◐	Endothelial nitric oxide synthase (eNOS) is the key enzyme responsible for maintaining vascular nitric oxide (NO) levels. Nitric oxide is responsible for the relaxation of blood vessels and reduced blood pressure. Individuals with one risk allele may have an increased risk of ischemic heart disease and ischemic stroke due to a reduced ability to synthesize nitric oxide.
MTHFR-C677T ▼	Involved in processing folate and converting homocysteine to methionine. Folate is necessary for proper homocysteine metabolism. A folate deficiency can cause homocysteine levels to rise. Elevated levels of homocysteine increase inflammation in the vascular system. This result has no increased risk for folate deficiency or elevated levels of homocysteine.
MTHFR-A1298C ▼	Involved in processing folate and converting homocysteine to methionine. Folate is necessary for proper homocysteine metabolism. A folate deficiency can cause homocysteine levels to rise. Elevated levels of homocysteine increase inflammation in the vascular system. This genotype results in decreased enzyme function but does not result in an increased risk of folate deficiency or elevated levels of homocysteine.
AGT ●	The angiotensin gene is involved in regulation of blood pressure. This result is often found to contribute to increased risk of coronary artery disease.
APOE ❍	ApoE is involved in the transport of cholesterol and fat molecules. This result is associated with a significantly lower ability to bind LDL receptors, higher ApoE levels, higher triglyceride levels, but lower cholesterol levels.
SLCO1B1*5 ●	Associated with the ability to metabolize statin medications, this result indicates poor metabolizer status with a significantly decreased ability to metabolize statins, lower response to statin therapy, and less LDL-C reduction with statin treatment. Consider routine creatine kinase (CK) monitoring. High dose statin therapy may not be advisable.

TREATMENT CONSIDERATIONS

Risk alleles from 9p21, AGT, eNOS T/T, MTHFR and APOE 4/4 may increase the risk of coronary artery disease. Annual monitoring of blood sugar, cholesterol, CRP and homocysteine is recommended. Elevated homocysteine may be addressed by supporting the methylation cycle with supplements such as methylfolate and methylcobalamin. Additionally, the BHMT (requiring choline) and CBS (requiring B6) pathways should be functioning properly. eNOS risk allele carriers may benefit from the addition of arginine and/or magnesium, as well as genistein under medical direction. EPA/DHA in the diet or as a supplement may be supportive. If lifestyle changes are not sufficient to lower cholesterol levels, consider using a fiber supplement, niacinamide, or fibrate medication rather than a statin medication.

ADDITIONAL COMMENTS

Risk alleles in this group can be supported with a plant-based diet low in saturated fats (such as the Mediterranean, Pritikin or Ornish diets). SLCO1B1*5 and APOE risk allele carriers may consider diets rich in fiber and plant sterols to help control cholesterol levels. MTHFR C677T risk allele carriers will benefit from eating a folate-rich diet (raw leafy greens) to support the breakdown of homocysteine. Stress management with deep breathing, meditation or exercise is recommended to reduce cardiovascular risk factors. Maintaining optimal BMI and blood sugar can reduce the risk for cardiovascular disease. Exercising 3-5 times a week for 30 minutes is also proven to improve heart health, as is maintaining optimal hydration.

PATIENT: PFirst PLast LAB ID NUMBER: 100000000HLA

Important Information About Your Nutrition Test Results

GC1/GC2	The GC gene produces the vitamin D binding protein which is responsible for transporting vitamin D to its target tissues. The T/A haplotype has an increased risk of vitamin D deficiency. The G/A haplotype is of low frequency in the general population and its clinical significance is unknown.
CYP2R1	This gene produces an enzyme that is responsible for the conversion of cholecalciferol to calcidiol as part of vitamin D synthesis. This result may be associated with lower serum vitamin D levels.
NADSYN1/DHCR7	This gene produces the enzyme 7-dehydrocholesterol reductase, which converts the vitamin D precursor (7-DHC) to cholesterol. This result may be associated with normal levels of serum vitamin D.
VDR-Bsm1	This gene produces a vitamin D receptor that is essential for promoting both calcium absorption, and maintenance of adequate serum calcium and phosphate levels to allow for proper mineralization of bone. This result may be associated with postmenopausal osteoporosis and bone mineral density disorders.
VDR-Taq1	Increasing evidence implicates vitamin D deficiency in less efficient endocrine and metabolic function. Polycystic ovary syndrome (PCOS) is a metabolic disease associated with insulin resistance, central adiposity, metabolic syndrome and infertility. Having one copy of the vitamin D receptor Taq1 C allele may be associated with increased risk for PCOS in some populations.
VDR-Fok1	Vitamin D has been identified as an important modulator of inflammation and endocrine function. The vitamin D receptor has been shown to be expressed in tumor tissues, suggesting that the receptor plays a role in cancer etiology. Multiple studies have identified FokI f (T) allele carriers as having an increased risk for ovarian, lung, and breast cancer.
TMPRSS6	This gene produces a protein called matriptase-2 which is part of a signaling pathway that controls the levels of another protein called hepcidin. Hepcidin is a key regulator of iron balance in the body. This result is associated with a potential risk for iron deficiency.
BCMO1	This gene produces the enzyme β,β-carotene 15,15'-monooxygenase 1 (BCMO1) which performs the first step in the metabolic conversion of carotenoids to retinol (vitamin A). This result is associated with a potential risk for vitamin A deficiency.
FUT2	The FUT2 enzyme is associated with vitamin B12 absorption from the gut. This result may be associated with higher serum vitamin B12 levels. Note: the FUT2 G is the secretor type.

TREATMENT CONSIDERATIONS

If carrying more than one risk allele for vitamin D deficiency (GC1/GC2, DHCR7/NADSYN, CYP2R1 and/or VDR-Fok1), consider regular vitamin D testing and increased frequency of vitamin D supplementation or exposure to sunlight. Prescription calcitriol may be considered for the CYP2R1 risk allele in partnership with calcitriol (1,25 dihydroxy-vitamin D) testing. Consider DEXA scan for VDR-Bsml risk allele carriers plus vitamin D3/K2 supplementation and lifestyle changes to support optimal bone mass density. BCMO1 risk allele carriers may benefit from supplementation with the active form of vitamin A, retinyl palmitate; food sources of retinyl palmitate include liver, egg yolks and fish. B-12 injections or sublingual B12 may be beneficial to patients carrying two FUT2 risk alleles. Optimizing digestion with digestive enzymes or other resources for increased nutrient absorption is recommended for all results.

ADDITIONAL COMMENTS

GC1/GC2 risk alleles, whether intermediate or elevated risk, may be supported by increased sunlight exposure; 15 minutes of full body exposure to sun daily or supplementation with vitamin D, along with monitoring serum vitamin D levels, may also support immune function as well as bone density. The TMPRSS6 risk allele, particularly in combination with two FUT2 risk alleles, can increase risk of anemia. A diet rich in iron with optimal gastrointestinal absorption may be beneficial, or supplementation may be required. A diet that is primarily plant-based with high quality lean meats for animal protein (particularly for cobalamin and retinyl palmitate) will support optimal nutrition.

PATIENT: PFirst PLast LAB ID NUMBER: 100000000HLA

Important Information About Your Graceful Aging Test Results

WNT16	◐	This gene makes a signaling protein that influences expression of genes associated with bone diseases and disorders such as osteoporosis. This result may be associated with risk of fracture or bone loss.
ESR1-1	◐	This gene produces an estrogen receptor which increases transcription of certain genes that play a role in sexual development, reproductive function, and tissue development such as bone. This result is associated with an undetermined risk for fracture or bone loss.
ESR1-2	❍	This gene produces an estrogen receptor which increases transcription of certain genes that play a role in sexual development, reproductive function, and tissue development such as bone. This result may be associated with a reduced risk of fracture.
COMT	=	The COMT enzyme inactivates catecholamines and converts catecholestrogens to methoxyestrogen, an anti-cancer metabolite. This result is associated with balanced enzyme activity which results in balanced dopamine and catecholestrogen levels.
CYP1A1	◐	This gene produces a cytochrome P450 enzyme that is responsible for drug and xenobiotic metabolism, particularly polycyclic aromatic hydrocarbons (PAHs). This result may be associated with increased susceptibility to xenobiotics and impaired DNA repair.
MAOA	◐	The MAOA enzyme is involved in the breakdown of the neurotransmitters serotonin, epinephrine, norepinephrine, and dopamine. These neurotransmitters regulate mood, emotion, sleep, appetite, and the body's response to stress. Therefore, MAOA may play a role in the development of depression. Studies examining MAOA and antidepressant response have shown that the C allele may be associated with a decreased response to antidepressants.
APOE	❍	The ApoE2 allele has a significantly lower ability to bind LDL receptors, and is associated with higher ApoE levels, higher triglyceride levels, but lower cholesterol levels. The ApoE2 allele has protective effects against Alzheimer's Disease.

TREATMENT CONSIDERATIONS

Estradiol is metabolized first by CYP1A1 into a cancer-promoting intermediate (catecholestrogen) and then by the COMT enzyme into a cancer-protective intermediate (methoxyestrogen). Individuals with reduced COMT activity may want to avoid estrogen replacement due to slower breakdown of genotoxic estrogens. A combined result of risk alleles resulting in a fast CYP1A1 (AG or GG) and a slow COMT enzyme (Met/Met) may cause a build-up of catecholestrogens, indicating increased need for antioxidants and healthy lifestyle changes. Supporting detoxification pathways may be warranted. COMT and MAOA have numerous biochemical relationships affecting the production of neurotransmitters and are best assessed together to determine treatment. Consider testing neurotransmitter levels to determine if supplementation is warranted. Optimal calcium, vitamin D and K2 may support bone health. Appropriate assessment of bone health and prevention of osteoporosis are indicated. High-dose DHA supplementation in ApoE4 carriers before the onset of AD dementia can be a promising approach to decrease the incidence of AD.

ADDITIONAL COMMENTS

A combination of WNT16 and ESR1 risk alleles may intensify the likelihood of fracture or bone loss. Weight-bearing exercise, stretching, and strength training support bone health and also help balance hormones and stabilize mood. An anti-inflammatory diet, low in refined sugars with low glycemic index foods, can help stabilize mood and support healthy weight goals. Meditation and exercise may help stabilize neurotransmitters. Increase daily fiber to 40-50 grams per day to help reduce cholesterol levels. ApoE risk allele carriers may benefit from dietary and lifestyle changes to support heart health and increased blood flow to the brain.

PATIENT: PFirst PLast LAB ID NUMBER: 100000000HLA

Important Information About Your Methylation Test Results

NOS-D298E ◐

Endothelial nitric oxide synthase (eNOS) is a key enzyme responsible for producing nitric oxide (NO). Nitric oxide is a signaling molecule that has been shown to play a role in cancer and heart disease, and is linked to altered cell metabolism. Individuals with this result may have reduced nitric oxide synthase activity.

MTHFR-C677T ▼

The MTHFR enzyme converts folate to the active form, 5-methylenetetrahydrofolate. Folate synthesis is required for remethylation of homocysteine to methionine. Elevated levels of homocysteine increase systemic inflammation. This result has no increased risk for folate deficiency or elevated levels of homocysteine.

MTHFR-A1298C ▼

The MTHFR enzyme converts folate to the active form, 5-methylenetetrahydrofolate. Folate synthesis is required for remethylation of homocysteine to methionine. Elevated levels of homocysteine increase systemic inflammation. Individuals with 2 risk alleles are associated with intermediate levels of enzyme activity but do not have an increased risk of folate deficiency or higher homocysteine levels.

CBS-A360A ◐

This gene produces an enzyme that uses vitamin B6 to convert homocysteine to cystathionine. This result is thought to have increased enzyme activity which may increase sulfates and ammonia and decrease levels of homocysteine and glutathione.

CBS-C699T ◐

This gene produces an enzyme that uses vitamin B6 to convert homocysteine to cystathionine. This result is thought to be associated with increased enzyme activity which may increase sulfates and ammonia and decrease levels of homocysteine and glutathione.

MTR-A2756G ◐

Methionine synthase is an enzyme that utilizes B12 to support the creation of methionine and resulting methyl donors. The MTR 2756 GG and AG genotypes are associated with lower folate concentrations and a higher risk of folate deficiency.

MTRR-A66G ◐

Methionine synthase reductase (MTRR) plays a critical role in one carbon metabolism by recycling methylcobalamin. One carbon metabolism is integral to DNA methylation. Aberrant DNA methylation and biosynthesis as a result of irregular one carbon metabolism is considered a mechanism in the development of cancer. A large number of studies have shown the MTRR A66G G allele is associated with an increased cancer risk in some populations. Having one allele of each may result in a slightly increased cancer risk.

TREATMENT CONSIDERATIONS

Certain allele combinations (MTHFR, MTR, MTRR) may increase the need for methylcobalamin and methylfolate beyond what is available in the diet. In these cases, targeted B12 and methylfolate supplementation may be beneficial. The combination of MTHFR, MTR, MTRR and CBS risk alleles may not result in elevated homocysteine due to the upregulation of CBS, but methyl donors may be deficient. Watch for pooling of methyl-donors with low serum homocysteine (the substrate for methionine production). Additionally, glutathione may be deficient due to CBS upregulation, requiring antioxidant and liver detox pathway support. Antioxidant therapy, specifically vitamins C and E, has been shown to improve endothelial function and may be indicated when eNOS risk alleles are present. Increased magnesium serum levels have been shown in numerous studies to affect endothelial function and potentially reduce risk of events such as ischemic stroke and endothelial dysfunction in end stage renal disease. In vitro studies suggest eNOS risk allele carriers may benefit from supporting nitric oxide production with arginine, magnesium and genistein under medical direction.

ADDITIONAL COMMENTS

MTHFR, MTR and MTRR rely on B12 for the continuation of the methionine cycle. 5-methyltetrahydrofolate has been shown to modulate eNOS which may result in increased nitric oxide production. Increased levels of eNOS inhibit MTR which may result in reduced methionine production and a potential decrease in methyl donors from SAMe. Furthermore, changes to the folate cycle affect the neighboring biopterin cycle. Reduced tetrahydrobiopterin availability limits nitric oxide production and increases the production of oxidative stressors in the form of superoxide. A diet high in raw leafy greens and animal protein will provide a balance of B vitamins and folate to support appropriate methylation. Optimizing blood flow with water consumption and appropriate exercise may be beneficial to eNOS risk allele carriers.

PATIENT: PFirst PLast

LAB ID NUMBER: 100000000HLA

How Your Test Results Relate To Other Areas of Health

MOOD

COMT	=
MTHFR-A1298C	▼
MTHFR-C677T	▼
MAOA	◐

Inefficient MTHFR enzyme activity may result in impaired folate availability and therefore reduced catecholamine and serotonin levels. The combination of COMT Val/Val and the C677T MTHFR risk allele may cause decreased SAMe levels. Folate is necessary for the biosynthesis of SAMe, the required methyl donor for neurotransmitter production. MTHFR efficacy may indirectly affect MAOA function downstream, resulting in changes to neurotransmitter levels. Both MAOA and COMT enzymes are responsible for decreasing dopamine levels in the brain. Estrogen impacts dopamine levels, as well as serotonin levels, through the regulation of COMT and MAOA enzymes. DRD2 and MTHFR C677T risk alleles independently increase risks for schizophrenia and bipolar disease; patients with these combined risk alleles should have increased monitoring for possible symptoms of these conditions.

BRAIN FUNCTION

APOE	○
NOS-D298E	◐
FUT2	○
MTHFR-C677T	▼

The ApoE risk allele is associated with increased risk of plaque formation in the brain and higher than normal levels of cholesterol. Healthy blood flow to the brain increases the oxygen supply to the cells. The eNOS risk allele is associated with higher blood pressure which can decrease circulation of oxygen-rich blood. The combination of ApoE and eNOS risk alleles could lead to an increased chance of plaque formation with reduced oxygen levels in the brain or increased vascular inflammation. In addition, the FUT2 risk allele could result in decreased B12 levels in the brain. A combination of eNOS and MTHFR risk alleles may result in increased vascular inflammation with a decrease in blood flow to the brain.

DIABETES

CYP2R1	◐
SH2B1	◐
MC4R	◐
9p21	○

All four risk alleles are associated with negative effects on the brain due to their impact on sugar metabolism and circulation. In particular, a combination of SH2B1 and MC4R risk alleles suggests monitoring of fasting blood glucose levels and HgA1C for early indication of the development of diabetes. A high fiber, low glycemic diet will support stable blood sugar levels. Additionally, fiber in the form of glucomannan has been shown to benefit fasting blood glucose as well as cholesterol levels and total body weight. The addition of the CYP2R1 polymorphism would suggest an increased requirement of vitamin D supplementation (potentially in the form of calcitriol with a provider's supervision) and monitoring. Diabetes is a significant risk factor for cardiovascular disease; in combination with the 9p21 risk allele there may be an increased risk of atherosclerosis.

B12 LEVELS

MTHFR-A1298C	▼
MTHFR-C677T	▼
MTR-A2756G	◐
MTRR-A66G	◐
FUT2	○

MTHFR risk alleles can reduce the amount of folate available. MTR and MTRR are involved in the production of methionine with the help of methylfolate and methylcobalamin. Changes in folate and B12 levels due to reduced enzyme activity may result in inefficiencies within the folate and methionine cycles. Vitamin B12 is important for energy, cardiovascular and bone health, nerve protection, regulating mood, and healthy cell repair. The FUT2 non-risk allele has been linked to increased absorption of vitamin B12. A diet high in raw leafy greens and animal protein will provide a balance of B vitamins and folate to support appropriate methylation; sometimes targeted B12 and methyl folate supplementation may be beneficial.