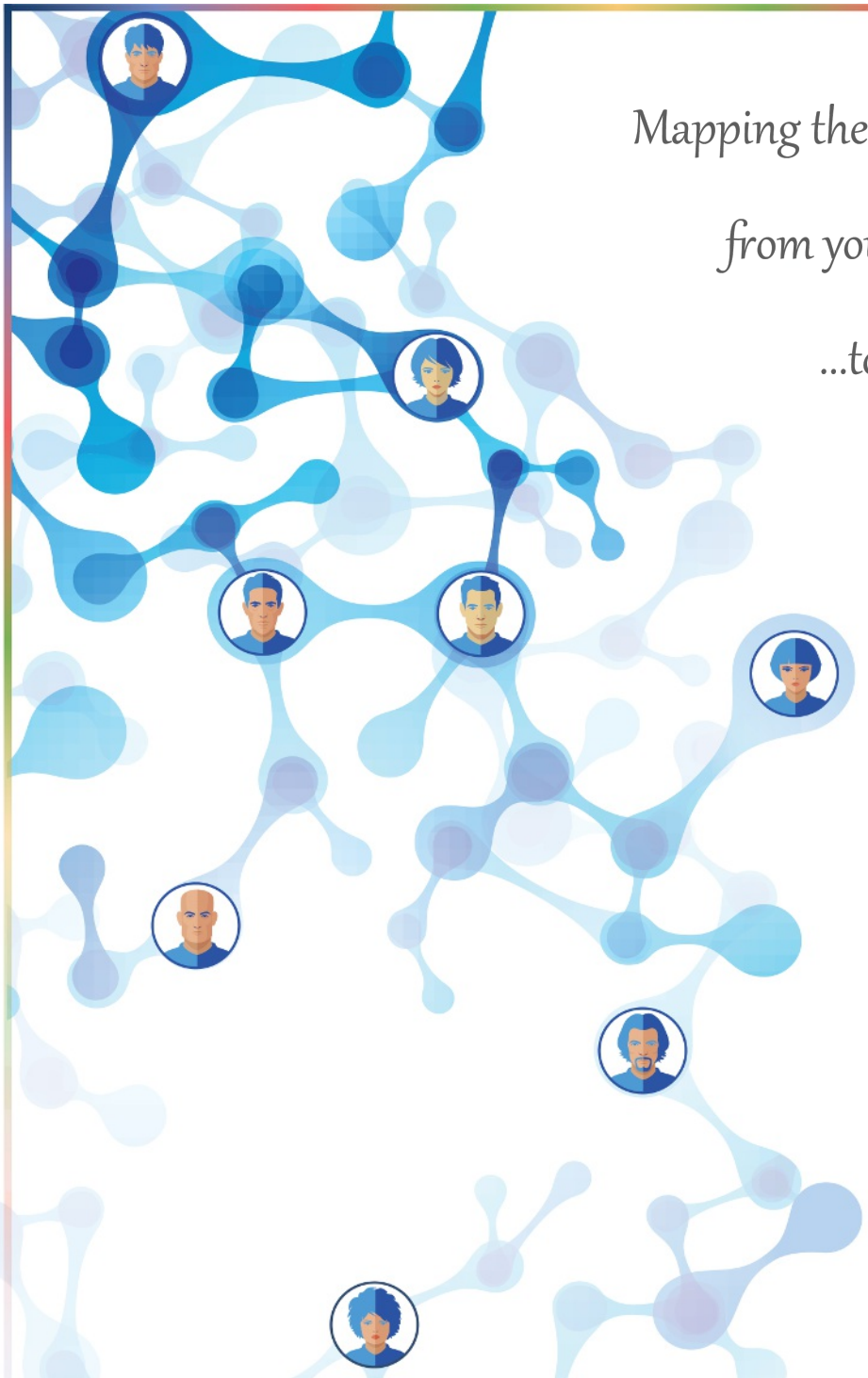

Mapping the path

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:	N8C9841
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
	DRD2	C/T		◐		Dopamine regulation, inflammatory response, eating behavior
	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
HEART	9p21	G/G			❍	Plaque formation in coronary arteries
	eNOS/NOS3	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
VITAMIN	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

**Combined genotype, read section detail for further explanation.*

NAME: PFirst PLast LAB ID NUMBER: N8C9841

Important Information About Your Weight Loss and Fitness 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.

DRD2 ◐

The DRD2 gene is part of the dopamine receptor system. This result may be associated with increased risk of inflammation, alcoholism, and, in conjunction with FTO, negative eating behavior.

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.

NAME: PFirst PLast LAB ID NUMBER: N8C9841

Important Information About Your Heart Health Test Results

9p21 ❍	This result is not associated with increased risk of coronary artery disease or atherosclerosis.
eNOS/NOS3 ◐	You may have an increased risk of heart disease or stroke caused by reduced blood flow because you carry one eNOS variant. 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.
MTHFR-C677T ▼	You have one variant in this gene. One variant reduces the MTHFR enzyme function which may slow down the absorption of folate. Folate is required for DNA synthesis, neurotransmitter production and detoxification among other things. Research has not found that one copy of this variant is a cause of elevated homocysteine or folate deficiency.
MTHFR-A1298C ▼	This genotype results in decreased enzyme function but does not result in an increased risk of folate deficiency or elevated levels of homocysteine. The C allele has also been associated with pediatric congenital heart defects.
AGT ●	Your gene increases your risk of coronary heart disease. Make diet and lifestyle a priority. Consult your doctor about niacin, essential fatty acids and resveratrol or medications depending on your symptoms.
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 ●	You do not metabolize statin drugs well. Talk with your doctor about alternative cholesterol lowering medications.

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, Niacin (nicotinic acid), 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.

NAME: PFirst PLast LAB ID NUMBER: N8C9841

Important Information About Your Vitamin Test Results

GC1/GC2	You may have an increased risk of vitamin D deficiency. This gene produces the vitamin D binding protein which is responsible for transporting vitamin D to its target tissues.
CYP2R1	You may have a mildly increased risk of vitamin D deficiency. This gene produces an enzyme that is responsible for helping to make the active form of vitamin D. Your enzyme may have decreased function.
NADSYN1/DHCR7	You may have normal levels of vitamin D. This gene produces an enzyme that is responsible for helping to make the active form of vitamin D. Your enzyme works normally.
VDR-Bsm1	You may have an increased risk of postmenopausal osteoporosis. This vitamin D receptor is essential to calcium absorption and calcium phosphate balance.
VDR-Taq1	You may have an increased risk for Polycystic Ovarian Syndrome (PCOS).
VDR-Fok1	When combined with other lifestyle and genetic factors, you may be at an increased risk for ovarian, lung and breast cancer.
TMPRSS6	You may have an increased risk for iron deficiency. This gene plays a part in the absorption of iron. You may have decreased absorption of iron.
BCMO1	You may have an increased risk for vitamin A deficiency. This gene produces an enzyme that is responsible for helping to make the active form of vitamin A called retinol. Your enzyme may have decreased function.
FUT2	You may not be at an increased risk for vitamin B12 deficiency. This gene product has an effect on the absorption of vitamin B12. NOTE: you are known as a secretor blood type.

NAME: PFirst PLast LAB ID NUMBER: N8C9841

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.

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Important Information About Your Graceful Aging Test Results

WNT16	◐	Your result may increase your risk of fracture or bone loss. The WNT16 gene is associated with bone diseases and disorders like osteoporosis.
ESR1-1	◐	Your result may be associated with an undetermined risk for fracture or bone loss. The ESR1 gene influences hormones like estrogen which play a role in tissue development such as bone.
ESR1-2	❍	Your result may be associated with a reduced risk of fracture. The ESR1 gene influences hormones like estrogen which play a role in tissue development such as bone.
COMT	=	Your result may be associated with a balanced breakdown of particular forms of the hormone estrogen and the neurotransmitter dopamine.
CYP1A1	◐	Your result may increase your reactivity to toxins or lead to reduced DNA repair. This gene plays an important role in eliminating drugs, toxins and estrogens.
MAOA	◐	Your result is not associated with any mood disorder but may lead to a reduced response to antidepressant medications. This gene is involved in the breakdown of neurotransmitters like adrenaline, dopamine and serotonin.
APOE	❍	Your result (the APOE2 allele) may have 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.

NAME: PFirst PLast LAB ID NUMBER: N8C9841

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.

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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.

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Defy Your DNA has added this page to maximize the information you can gain from your genes.

How To Read This Page:

Use the genotype risk key for each set of genes to see what your combination of risks are for every section. This will let you know if you are at partial or high risk. Lifestyle recommendations are for all risk genes including yours.

MOOD

DRD2	◐
COMT	=
MTHFR-A1298C	▼
MTHFR-C677T	▼
MAOA	◐

- If you have risk alleles for MTHFR, one of the pathways that uses folate may not be working properly. In this case, your ability to make neurotransmitters may influence the risk of depression, schizophrenia and bipolar disorder.
- If you have COMT Val/Val and the C677T MTHFR risk alleles there may be impaired dopamine signaling in the brain resulting in mood instability.
- MTHFR may indirectly interact with MAOA which leads to neurotransmitter imbalance and has been associated with depression in menopausal women.
- Both MAOA and COMT enzymes are responsible for decreasing dopamine levels in the brain. If you have risk alleles in these genes, you may want to work on balancing your neurotransmitters with diet, meditation and exercise.
- Estrogen impacts dopamine levels, as well as serotonin levels, through the regulation of COMT and MAOA enzymes.

DIABETES

MC4R	◐
SH2B1	◐
CYP2R1	◐
9p21	○

- All four risk alleles are associated with negative effects on the brain due to their impact on sugar metabolism and circulation.
- If you have a combination of the SH2B1 and the MC4R risk alleles you might consider monitoring your fasting blood glucose levels and HbA1C to catch signs of diabetes early.
- A high fiber, low glycemic diet will help to stabilize your blood sugar levels.
- You may consider trying fiber in the form of glucomannan because it has been shown to benefit fasting blood glucose as well as cholesterol levels and total body weight.
- If you also have the CYP2R1 polymorphism you may require increased 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; The 9p21 risk allele may put you at an increased risk of atherosclerosis.

BRAIN FUNCTION

APOE	○
eNOS/NOS3	◐
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. Increased plaque in the brain is associated with Alzheimer's disease and dementia.
- 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 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.

B12 LEVELS

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

- MTHFR risk alleles can reduce the amount of folate available which can prevent B12 from being utilized.
- FUT2 risk alleles can alter the amount of B12 available to cells.
- Changes in folate and B12 levels may influence energy, cardiovascular and bone health,nerve protection, mood regulation, 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 allow the body to use B12.
- Sometimes targeted B12 and folate supplementation may be beneficial.