NUTRIGENOMICS **REPORT**

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Genetics Report

The Function of Genetics In Health & Disease

Genetics can play key roles in disease process development.

It is significant to address that with any discussion regarding genetic mutations, gene expression is controlled by epigenetic regulation. The epigenome is strongly influenced by: diet, toxicity and environmental factors.

Most of the time, our genetic mutations are not expressive, they are silenced by epigenetic controls. Therefore, not all genetic mutations may be a problem.

Symptomatic association and correlation with lab testing is a very viable and useful means to understanding the expression of certain gene mutations.

Each gene has dozens, hundreds or thousands of variations. These are known as SNPs (singular nucleotide polymorphisms). Genes work by coding enzymes. Think of this as a copying system. The original mold (gene sequence) transcribes a duplicate in the form of RNA, which then encodes a specific enzyme. Enzymes then function to generate biochemical reactions in various processes in the body.

If certain gene mutations are expressive, the enzymes that the gene encodes may be absent, not fully functional, or in some instances “over-expressive”. This altercation of function is a core component with how gene mutations are involved in symptoms and disease processes.

Therapies to nutritionally support genetic mutations is known as nutrigenomics. This is where certain nutrients are given in order to provide support for expressive gene mutations.

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How To Use This Report

This report is non-diagnostic and can in no way be used as a diagnosis for any disease or health condition.

This report serves as an evaluation of many genes and genetic SNPs. It is a starting point to understand inherited strengths and weaknesses.

This report is grouped into specific categories according to how certain genes affect certain biological functions.

You will notice that certain gene SNPs are found in more than one category. This is because certain genes can influence numerous biological functions.

APOE

These are SNPs used to determine APOE genotype through applying a set of rules to identify ”genosets ” described here: http://snpedia.com/index.php/ APOE.

RS#	Call	Risk Allele	Gene	Variation	Result
rs429358	TT	C	APOE		-/-
rs7412	CC	C	APOE	Arg176Cys	+/+

Determined APOE genotype: **3/3**

This APOE genetics section analyzes the 2 most influential SNPs that determine APOE status.

Apolipoprotein E is a protein involved in lipid metabolism. Variations of APOE significantly influence risk for cardiovascular disease and Alzheimer’s. APOE significantly interacts with the LDL receptor and mediates levels of LDL and triglyceride.

The “APOE 4/4” genotype has the highest Alzheimer’s disease risk, compared to all of the other APOE genotypes.

For a more extensive discussion on APOE status go here (R)

Autism-Related Genetics

This section analyzes various genes associated with autism spectrum, such as those influencing neurotransmitters, behavior, and detoxification.

RS#	Call	Risk Allele	Gene	Variation	Result
rs1800498	AA	A	DRD2		+/+
rs4532	CT	T	DRD1		+/-
rs686	AG	A	DRD1		+/-
rs265981	AG	G	DRD1		+/-
rs662	CT	C	PON1	Q192R	+/-

DRD1 - Dopamine receptor D1 is essential in the utilization of the neurotransmitter dopamine.

The risk allele A for rs686 is associated with nicotine dependence (R), alcohol dependency and alcohol withdrawal-induced seizures (R).

Rs686 A allele is part of the C-A-T haplotype in autism in ‘male-only’ populations studied (R). The C-A-T haplotype consists of the following SNPs and their respective alleles: rs2655981 (G), rs686 (A), rs4532 (A). (R)

Rs265981 has been studied with autism association in a ‘male only’ population with 2 or more affected males. The C allele (reported in 23andme as ‘G’) is the risk and is part of the C-A-T haplotype (R). Affected individuals with the C-A-T phenotype display greater difficulties with non-verbal communication, social interactions, and increased stereotypies.

DRD2 - Dopaminergic receptor D2 is essential in the utilization of the neurotransmitter dopamine.

In a study looking at autism in families with 2 or more male siblings, the Rs1800498 AA risk allele was found with a significantly increased frequency in affected individuals, and with more severe problems with social interaction and communication (R).

FGA - Fibrinogen alpha chain is involved in the coagulation cascade. The risk allele C is strongly associated with autism spectrum among Korean populations (R).

PON1 - Paraoxonase 1 is a gene involved in detoxification of environmental chemicals such as parathion and organophosphates. Paraoxonase influences arylesterase, which catalytically degrades BPA (bisphenol A), protects against LDL oxidation and removes lipid peroxides. Rs662 of PON1 affects the rate of hydrolysis of a number of organophosphates.

Rs rs662 was studied in relation to autism and serum levels of arylesterase. For the Italian population, the CC genotype for rs662 featured significantly lower arylesterase levels among ASD patients compared to the TT genotype. For caucasian-Americans, the CC genotype for rs662 featured lower arylsterase levels but not as dramatic as the Italian population (R).

Alarmingly, literature has identified that PON1 expression is lower in newborns compared to adults. It has been known since 1983 that developing fetuses have 7-fold lower PON1 activity in cord blood compared to levels in adults. (R). This implies organophosphate toxicity of the mother may have significant deleterious consequences on the developing fetus and on neonates, as several organophosphates such as chlororpyrifos can cross the placenta.

For PON1 variant rs662, Caucasian and African American mothers with the CC genotype showed the lowest PON1 enzyme activity (Mean PON1 enzyme activity: 122.7) compared to the AA genotype (Mean PON1 enzyme activity: 138.1) (R).

NOTE: Rules of PON1 Q192R variant genotyping. R=G and G is represented in 23andme as C. Q=A and A is represented in 23andme as T.

Brain Health Genetics

Brain health genetics analyzes various genes related to brain function. These include genes related to: neurotransmitter synthesis & breakdown, brain antioxidants, and methylation genes.

RS#	Call	Risk Allele	Gene	Variation	Result
rs1801131	TT	G	MTHFR	A1298C	-/-
rs1801133	GG	A	MTHFR	C677T	-/-
rs3741775	CC	C	DAO		+/+
rs2070586	GG	A	DAO		-/-
rs6323	T	T	MAO A	R297R	+/-
rs2519152	CT	C	DBH		+/-
rs1108580	AG	A	DBH		+/-
rs1611115	CC	T	DBH		-/-
rs4680	AA	A	COMT	V158M	+/+
rs4633	TT	T	COMT	H62H	+/+
rs769224	GG	A	COMT	-61 P199P	-/-
rs701492	CC	T	GAD1		-/-
rs3828275	CC	T	GAD1		-/-
rs10432420	GG	A	GAD1		-/-
rs3791878	GT	T	GAD1		+/-
rs12185692	CC	A	GAD1		-/-
rs3791850	GG	A	GAD1		-/-
rs3791851	TT	C	GAD1		-/-
rs2058725	TT	C	GAD1		-/-
rs769407	GG	C	GAD1		-/-
rs2241165	TT	C	GAD1		-/-
rs3749034	GG	A	GAD1		-/-

GAD1 (Glutamate decarboxylase) — Involved in conversion of glutamate to GABA. Mutations are seen in glutamate excitotoxicity, GABA deficiency.

COMT (catechol-O-methyltransferase) — Involved in the breakdown of dopamine & norepinephrine. Mutations seen in behavioral disorders, and may involve abnormal

concentrations of serotonin and norepinephrine.

DBH (Dopamine Beta Hydroxylase) — Involved in the conversion of dopamine into norepinephrine. Copper and ascorbic acid are the cofactors. rs1611115-T has shown a strong inverse correlation to plasma dopamine beta-hydroxylase levels.

MAO-A (Monamine oxidase) — Involved in the breakdown of serotonin. Mutations seen in mood/behavior issues. May lead to abnormal serotonin.

DAO (di-amino oxidase) — Enzyme involved in the degradation of histamine. Involved in dopamine synthesis. Regulates L-Serine in the brain. Mutations are seen in schizophrenia & bi-polar disorders. Histamine is an immune compound as well as a neurotransmitter.

MTHFR (Methylene tetrahydrofolate reductase) — Involved in the formation of 5-methyl folate. The active, methylated folate is central to methylation cycle function, and the “remethylation” of homocysteine. Mutations in MTHFR genes (especially C677T and A1298C variants) may significantly reduce the rate of homocysteine methylation, leading to an elevation in homocysteine levels, which is a major risk factor for cardiovascular inflammation. MTHFR also participates in neurotransmitter synthesis by contributing methyl donors to the biopterin (BH4) cycle.

Clotting Factors

Clotting factor genetics analyzes various genes related to the clotting systems. These may be related to: lipid esters, thrombin formation, platelet aggregation, heparin binding and Vitamin K-related clotting factors.

RS#	Call	Risk Allele	Gene	Variation	Result
rs6048	A	G	F9	G580A	-/-
rs6025	CC	T	F5	Factor V Leiden	-/-
i3002432	GG	A	F2	Prothrombin G20	-/-
rs6046	GG	A	F7	A353G	-/-
rs3211719	AG	G	F10	113777509A>C(?)	+/-
rs2289252	CC	T	F11		-/-
rs9898	CC	T	HRG		-/-
rs2227589	CC	T	SERPINC1		-/-
rs1523127	CC	C	NR1I2		+/+
rs2731672	TT	T	KNG	I598T(?)	+/+
rs5918	TT	C	ITGB3	T196C	-/-
rs1613662	AA	G	GP6		-/-
rs13146272	AC	C	CYP4V2		+/-
rs1800775	AA	C	CETP		-/-

CETP - (Cholesteryl Ester transfer protein) — Involved in lipid transport. Reverse transport of cholesterol esters.

CYP4V2 - (cytochrome P450 family) — Involved in eye health, electron transport & hydroxylation of saturated fatty acids.

GP6 (Glycoprotein 6) – Involved in platelet activation & adhesion. Important as an activator of thrombin, prothrombin, and fibrinogen. May play a role in cervical cancer and chronic cervicitis.

ITPG3 (Platelet glycoprotein 3) – This gene encodes a receptor enzyme of numerous clotting proteins. This enzyme also functions to form various adhesion proteins and is involved in cell signaling for cell growth, differentiation, survival, and cell programmed death (apoptosis).

KNG1 (kininogen) — Involved in blood clotting. GP6 (Glycoprotein 6) — Involved in collagen-induced platelet aggregation. May play a role in cervical cancer and chronic

cervicitis.

NR1I2 - (Nuclear receptor sub family 2) — Binds to CYP class. Involved in the degradation of xenobiotics.

SERPINC1 (Serpin peptidase inhibitor Clade C) — Involved in thrombin inhibition and is a plasma protease inhibitor.

F11 (Coagulation factor XI) — involved in blood coagulation. Presents as a zymogen.

HRG (Histidine rich glycoprotein) — Heparin and ligand-binding protein.

F10 (Coagulation Factor 10) — Vitamin K-dependent clotting factor involved in the conversion of prothrombin to thrombin.

F2 (Coagulation factor II) — First step in the coagulation cascade.

F5 (Coagulation factor 5) - Involved in the formation of thrombin from prothrombin.

F9 (Factor 9) — Involved in calcium and phospholipid channel-induced clotting.

Detoxification Genetics

Detoxification is the cellular process of breaking down and removing potentially harmful substances. These substances may be environmental chemicals, toxic metals, or the prevention of free radical formation. In most systems, there are 2 cycles of detoxification reactions, referred to as “phase 1” and “phase 2”. Each phase consists of various stages, such as reduction, conjugation, hydroxylation, sulfation, methylation, glucoronidation, glutathione conjugation.

Detoxification — CYP (cytochrome P450)

RS#	Call	Risk Allele	Gene	Variation	Result
rs4986910	AA	G	CYP3A4*3	M445T	-/-
rs2740574	TT	G	CYP3A4*1B		-/-
rs6413419	GG	A	CYP2E1*4	A4768G	-/-
rs2070676	CC	G	CYP2E1*1B	G9896C	-/-
rs16947	GG	A	CYP2D6	T2850C	-/-
rs1065852	GG	A	CYP2D6	T100C	-/-
rs1135840	CC	C	CYP2D6	S486T	+/+
rs1057910	AA	C	CYP2C9*3	A1075C	-/-
rs1799853	CC	T	CYP2C9*2	C430T	-/-
rs12248560	CC	T	CYP2C19*17		-/-
rs1801272	AA	T	CYP2A6*2	A1799T	-/-
rs10012	CG	C	CYP1B1	R48G	+/-
rs1800440	TT	C	CYP1B1	N453S	-/-
rs1056836	CG	C	CYP1B1	L432V	+/-
rs762551	AA	C	CYP1A2	C164A	-/-
rs1799814	GG	T	CYP1A1*4	C2453A	-/-
rs1048943	TT	C	CYP1A1*2C	A4889G	-/-

CYP family (cytochrome P450) – Involved in phase 1 detoxification reactions. CYPs are found in most cells and are heavily concentrated in liver cells.

CYP’s function is to trigger metabolic reactions related to:

- Degradation of chemical toxins
- Steroid hormone synthesis & degradation
- Drug metabolism

- Synthesis & metabolism of cholesterol

There are thousands of CYP genes. Currently, the literature suggests that various forms of carcinogenesis risk exist among the various CYP gene mutations.

Detoxification — Misc SNPs

RS#	Call	Risk Allele	Gene	Variation	Result
rs1800566	GG	A	NQO1		-/-
rs1105879	AC	C	UGT1A6	552AC	+/-
rs6759892	GT	G	UGT1A6	Ser7Ala	+/-
rs2070959	AG	G	UGT1A6	T181A	+/-
rs4148325	CT	T	UGT1A1		+/-
rs887829	CT	T	UGT1A1		+/-
rs6742078	GT	T	UGT1A1		+/-
rs1799895	CC	G	SOD3		-/-
rs671	GG	A	ALDH2		-/-
rs4880	AA	G	SOD2	A16V	-/-
rs2855262	CT	T	SOD2		+/-
rs2758331	CC	A	SOD2		-/-
rs1801280	TT	C	NAT2	T341C (I114T)	-/-
rs1799931	GG	A	NAT2	G857A (G286E)	-/-
rs1799930	AG	A	NAT2	G590A (R197Q)	+/-
rs1805158	CC	T	NAT2	C190T (R64W)	-/-
rs1208	AA	G	NAT2	A803G (K268R)	-/-
rs4986782	GG	A	NAT1	A560G(?) (R187Q	-/-
rs1138272	CC	T	GSTP1	A114V	-/-
rs1695	AA	G	GSTP1	I105V	-/-
rs1056806	CC	T	GSTM1		-/-
rs662	CT	C	PON1	Q192R	+/-

ALDH2 (Aldehyde dehydrogenase) — Involved in the detoxification of alcohol, specifically in the oxidation of aldehydes into carboxylic acids. Deficiency of ALDH2 enzyme activity is believed to increase levels of acetaldehyde, and contribute to its toxicity.

GSTM1 (Glutathione transferase) - Involved in phase 2 detoxification & degradation of toxins, xenobiotics, and carcinogens. GSTM1 expression is believed to be highly expressed in the liver.

GSTP1 (Glutathione transferase) – Involved in phase 2 detoxification & degradation of toxins, xenobiotics, and carcinogens.

NAT1 family (N-acetyltransferase) - Involved in acetylation detox cycles. Acetylation is a phase 2 detoxification reaction. Mutations in NAT1 may increase the likelihood of drug-induced hepatitis and may predispose towards multiple chemical sensitivities.

NAT2 family (N-acetyltransferase) — Involved in the acetylation detox cycles. Acetylation is a phase 2 detoxification reaction. NAT2 mutations reportedly reduce the turnover of acetylation detoxification and may alter the metabolism of certain drugs.

NQO1 - Quinone oxidoreductase - NQO1 detoxifies semi-quinones, which in some forms act as DNA mutagens. NQO1 is essential in the detoxification of various environmental toxins such as benzene. Homozygosity for rs1800566 is associated with elevated benzene toxicity.

PON1 (Paraoxonase) — Protein degrades organic chemicals and pesticides, such as parathion. PON1 enzymes prevent LDL oxidation and may be cardioprotective against atherosclerotic plaque. PON1 is also involved in the cardioprotective anti-oxidant activities of HDL.

SOD2 (superoxide dismutase) — Mitochondrial antioxidant of the manganese class, involved in detoxification.

SOD3 - Superoxide dismutase-3 is an antioxidant that quenches the superoxide anion. Homozygosity of rs1799895 is associated with a higher risk of ischemic heart disease (R)

UGT1A1 - UDP-glucuronsyltransferase is integral to glucuronidation, a phase 2 detoxification reaction, which involves the addition of a glucuronide to molecules such as hormones, bilirubin, toxins and drugs making them water soluble for excretion. The risk allele for rs6742078 is associated with Gilbert's syndrome, higher bilirubin levels, and may also increase the risk for gall stones (R). Impaired glucuronidation may reduce the capacity to appropriately biotransform and metabolize a variety of compounds, and thus reduce the liver's capacity to remove xenobiotics, hormones, drugs and bilirubin. Individuals with the risk allele for rs6742078, rs887829 and/or rs4148325 tend to have higher levels of unconjugated bilirubin, and may also have higher levels of 17ß-Estradiol, and possibly higher levels of thyroid hormones due to the fact that glucuronidation controls levels of T4.

UGT1A6 - UDP-glucuronsyltransferase is integral to glucuronidation, a phase 2 detoxification reaction, which involves the addition of a glucuronide to molecules such as hormones, bilirubin, toxins and drugs making them water soluble for excretion. The variants rs2070959, rs6759892, and rs1105879 are significantly associated with a high

risk of gall stone-related cholecystectomy, and elevated levels of bilirubin in elderly subjects (R).

Homozygotes for UGT1A1 and UGT1A6 variants should consider routine bilirubin blood testing and consider therapeutic maintenance to support hepatic glucuronidation function. Gilbert's syndrome is also associated with porphyrin abnormalities in white blood cells (R). Literature does support the hypothesis that higher levels of bilirubin may confer protective effects against the risk of certain cancers, however, this is at the expense of decreased glucuronidation.

Detoxification — Sulfation

RS#	Call	Risk Allele	Gene	Variation	Result
rs11083907	GG	A	SULT2A1		-/-
rs2547231	AC	C	SULT2A1		+/-
rs4149449	CT	T	SULT2A1		+/-
rs4149452	CC	T	SULT2A1		-/-
rs11569679	CC	T	SULT2A1		-/-
rs296366	CT	T	SULT2A1		+/-
rs7192559	CC	T	SULT1A1		-/-
rs4149381	TT	G	SULT1A1		-/-
rs60701883	CC	A	SULT1A1		-/-
rs4149385	CC	T	SULT1A1		-/-
rs1042008	GG	A	SULT1A1		-/-
rs9282862	TT	C	SULT1A1		-/-
rs60749306	TT	C	SULT1A1		-/-
rs36043491	CC	T	SULT1A1		-/-
rs1042157	GG	A	SULT1A1		-/-
rs35728980	TT	G	SULT1A1		-/-

SULT1A1 (Sulfotransferase family cytosolic 1A) — Involved in sulfation detoxification reactions: degradation of xenobiotics, hormones, neurotransmitters, and toxins.

SULT2A1 (Sulfotransferase family cytosolic 2A DHEA) — Involved in sulfation detoxification reactions. Catalyzes the sulfation of bile acids and steroid hormones in the liver and adrenal glands. May be involved in androgen- driven PCOS

Estrogen Metabolism Genetics

Estrogen Metabolism Genetics analyzes various genetic factors related to the hydroxylation, methylation and metabolism of the estrogens. These genes can be found in association to various estrogen metabolites, such as: 2OHE1, 4OHE1, 16aOHE1, and various methoxy estrogens.

RS#	Call	Risk Allele	Gene	Variation	Result
rs6742078	GT	T	UGT1A1		+/-
rs55785340	AA	G	CYP3A4*2		-/-
rs1004982	TT	C	CYP19A1		-/-
rs727479	AA	A	CYP19A1		+/+
rs749292	AG	A	CYP19A1		+/-
rs4986883	TT	C	CYP19A1		-/-
rs1056806	CC	T	GSTM1		-/-
rs4986910	AA	G	CYP3A4*3	M445T	-/-
rs2740574	TT	G	CYP3A4*1B		-/-
rs12248560	CC	T	CYP2C19*17		-/-
rs10012	CG	C	CYP1B1	R48G	+/-
rs1800440	TT	C	CYP1B1	N453S	-/-
rs1056836	CG	C	CYP1B1	L432V	+/-
rs762551	AA	C	CYP1A2	C164A	-/-
rs1799814	GG	T	CYP1A1*4	C2453A	-/-
rs1048943	TT	C	CYP1A1*2C	A4889G	-/-
rs4680	AA	A	COMT	V158M	+/+
rs4633	TT	T	COMT	H62H	+/+

CYP1A2 — Participates in the hydroxylation of Estrone (E1) into 2-OH-E1 and 4-OH-E1. CYP1A2 also catalyzes the formation of Estradiol (E2) into 2-OH-E2.

CYP1A1 — Participates in the hydroxylation of Estrone into 2-OH-E1 and 16-OH-E1.

CYP1B1 — Participates in the hydroxylation of Estrone into 2-OH-E1 and 4-OH-E1. Additionally, the CYP1B1 L432V variant has been shown to influence both the 2-OHE1/16-OH-E1 ratio, as well as the 4-OH-E1/2-OH-E1 ratio.

CYP2C19 — Mutations in this gene are believed to increase the catabolism of estrogen,

and may lead to lower estrogen levels.

CYP19A1 — This gene encodes for aromatase, which converts androgens into estrogens. For variants rs749292 and rs727479, the A (+) allele is considered an “upregulation” of aromatase activity and has been associated with 10-20% increases in circulating estrogen in postmenopausal women.

CYP3A4 — Participates in the hydroxylation of Estradiol (E2) into 2-OH-E2. CYP3A4 also catalyzes the formation of the potentially carcinogenic 16 alpha- OH-E1.

GSTM1 — Involved in the synthesis of the enzyme GST (glutathione-S- transferase), which synthesizes the reduced form of glutathione.

COMT (catechol-O-methyltransferase) — Involved in the methylation of dopamine, noradrenaline, as well as estrogens.

UGT1A1 - UDP-glucuronsyltransferase is integral to glucuronidation, a phase 2 detoxification reaction, which involves the addition of a glucuronide to molecules such as hormones, bilirubin, toxins and drugs making them water soluble for excretion. The risk allele for rs6742078 is associated with Gilbert’s syndrome, higher bilirubin levels, and may also increase the risk for gall stones (R). Impaired glucuronidation may reduce the capacity to appropriately biotransform and metabolize a variety of compounds, and thus reduce the liver’s capacity to remove xenobiotics, hormones, drugs and bilirubin. Individuals with the risk allele for rs6742078, rs887829 and/or rs4148325 tend to have higher levels of unconjugated bilirubin, and may also have higher levels of 17ß-Estradiol, and possibly higher levels of thyroid hormones due to the fact that glucuronidation controls levels of T4.

Fatty Acid & Lipid Metabolism

Fatty acid metabolism genes are related to fatty acid desaturases, the activities of Omega 6 fatty acids such as arachidonic acid, omega 3 fatty acids such as EPA and DHA. This section also concerns phospholipid metabolism such as choline.

Choline-Related

RS#	Call	Risk Allele	Gene	Variation	Result
rs7946	TT	C	PEMT		-/-
rs4646406	AT	A	PEMT		+/-
rs4244593	GT	T	PEMT		+/-
rs868750	AG	G	CHAT		+/-
rs1880676	GG	G	CHAT		+/+
rs1799807	TT	C	BCHE	D70G	-/-
rs1803274	CT	T	BCHE		+/-

BCHE - Butyrylcholinesterase is a cholinesterase enzyme that hydrolyzes a variety of choline esters, including the breakdown of the neurotransmitter acetylcholine. BCHE has been studied in relationship to Alzheimer's disease. rs1803274 is known as the "K" allele, and the risk allele is known to reduce the function of the BCHE enzyme by 33% (R). Carriers of TT for rs1803274 have shown to carry 2-3.5x higher Alzheimer's risk (R). Rs1799807 affects the structure, function and substrate specificity of the BCHE gene. The risk allele for rs1799807, may increase adverse events from:

- Cholinesterase-inhibiting drugs
- Succinylcholine (an anesthetic drug)
- Nightshade foods
- Pesticides on foods, including organophosphates
- Nerve gasses such as Sarin and VX gasses

(R)

CHAT - choline acetyltransferase is a gene that provides instructions for making the neurotransmitter acetylcholine from the B-vitamin choline. Acetylcholine is a primary neurotransmitter of the parasympathetic nervous system, including the vagus nerve.

The GG genotype for rs1880676, rs1880676 and rs868750 is associated with Alzheimer's disease. A 2006 study found of 563 Alzheimer's patients, 56.2% carried the GG risk allele for rs1880676, whereas with rs3810950 56.3% of carriers of the GG genotype had Alzheimer's, and for rs868750, 63.5% of the GG genotype had Alzheimer's (R).

PEMT - Phosphatidylethanolamine methyltransferase is involved in the conversion of the

phospholipid ethanolamine into phosphatidylcholine. Phospholipids are components of cellular membranes, and facilitate vital functions in the brain, liver, intestines and nervous system.

Fatty Acid Desaturase

RS#	Call	Risk Allele	Gene	Variation	Result
rs1535	AG	G	FADS2		+/-
rs174548	CG	G	FADS1		+/-
rs174537	GT	G	FADS1		+/-

FADS1 & FADS2 - Fatty acid desaturases are involved in the unsaturation of fatty acids. FADS1 is integral in the formation of omega 6 arachidonic acid (AA) and omega 3 eicosapentanoic acid (EPA). FADS1 is also strongly associated with ceramide and sphingomyelin metabolism (R), which are important structural cell membrane lipids.

rs174537 status significantly influences arachidonic acid, LDL-C and EPA levels (R). The risk allele is associated with higher levels of LDL-C, AA and all other PUFAs (polyunsaturated fatty acids) except for linoleic acid. rs174537 accounts for a 19% overall variation in arachidonic acid levels.

rs174548 risk allele is associated with lower phosphatidylcholine values. Phosphatidylcholine is essential for liver and gall bladder function, bile acid formation and for cell membrane fluidity of every cell of the body.

Individuals with risk alleles in the fatty acid desaturase section may wish to monitor blood spot RBC fatty acid profiles, which tests the AA/EPA ratio. This may be especially useful with chronic inflammation and conditions of autoimmunity.

GI Health Genetics

GI Health Genetics analyzes various genes that have been studied to influence the health of the GI tract. Some of these processes include: gut flora activity, vitamin B-12 utilization, phospholipid activity, and various GI- related immune responses.

RS#	Call	Risk Allele	Gene	Variation	Result
rs4728142	AG	A	IRF5		+/-
rs10210302	CT	C	ATG16L1		+/-
rs34095989	GG	A	SHMT2		-/-
rs7946	TT	C	PEMT		-/-
rs4646406	AT	A	PEMT		+/-
rs4244593	GT	T	PEMT		+/-
rs558660	GG	A	GIF (TCN3)		-/-
rs602662	AG	A	FUT2		+/-
rs601338	AG	A	FUT2		+/-
rs492602	AG	G	FUT2		+/-

(Fucosyltransferase 2) — Involved in H antigen formation through oligosaccharide FuC alpha. Associated with intestinal flora imbalance & Crohn's disease. Mutations in FUT2 may predispose towards low concentrations of bifidobacterium. FUT2 may also be involved in Vitamin B-12 levels.

GIF (Gastric intrinsic factor) — Involved in the formation of intrinsic factor for B-12 utilization. Intrinsic factor is produced by the parietal cells of the stomach.

PEMT (phosphatidylethanolamine methyltransferase) — Involved in the conversion of the phospholipid ethanolamine into phosphatidylcholine. Phospholipids are components of cellular membranes, and facilitate vital functions in the brain, liver, intestines and nervous system.

SHMT (serine hydroxymethyltransferase) — Involved in purine synthesis via folate derivatives. Mutations may involve abnormal iron metabolism & predisposition to GI pathogens.

ATG16L1 (Autography related 16 like 1) — Involved in the lysozyme degradation of cells. Mutations are seen in IBS and Crohn's disease. ATG16L1 is involved in the conjugation of phosphatidylethanolamine.

IRF5 (Interferon Regulatory Factor) — Involved in the formation of antiviral cytokine interferon. May be involved in switching macrophages to increase or decrease interferon

production. Mutations are seen in IBS, scleroderma.

Heart Health Genetics

Heart Health Genetics analyzes various genes related to cardiovascular function. These include genes related to: homocysteine, inflammatory activity, specific antioxidants, nitric oxide, methylation genetics and mitochondrial genetics related to coenzyme Q10.

RS#	Call	Risk Allele	Gene	Variation	Result
rs2229765	AA	A	IGF1R		+/+
rs809359	AG	G	NDUFS7		+/-
rs7258846	GT	T	NDUFS7		+/-
rs1142530	CT	T	NDUFS7		+/-
rs2332496	AG	A	NDUFS7		+/-
rs3754822	AG	A	CoQ10B		+/-
rs3918188	AC	A	NOS3		+/-
rs1800779	AG	G	NOS3		+/-
rs1800783	AT	A	NOS3		+/-
rs2248814	GG	A	NOS2		-/-
rs2274894	GG	T	NOS2		-/-
rs2297518	AG	A	NOS2		+/-
rs11982486	TT	C	PON2		-/-
rs7493	CG	G	PON2	Ser311Cys	+/-
rs662	CT	C	PON1	Q192R	+/-
rs1802059	GG	A	MTRR-11	A664A	-/-
rs1801394	GG	G	MTRR	A66G	+/+
rs4920037	GG	A	CBS	C19150T	-/-
rs2851391	CC	T	CBS	A13637G	-/-
rs1801181	AA	A	CBS	A360A	+/+
rs234706	GG	A	CBS	C699T	-/-
rs1801131	TT	G	MTHFR	A1298C	-/-
rs1801133	GG	A	MTHFR	C677T	-/-

MTHFR (Methylene tetrahydrofolate reductase) — Involved in the formation of 5-methyl folate. The active, methylated folate is central to methylation cycle function, and the “remethylation” of homocysteine. Mutations in MTHFR genes (especially C677T and

A1298C variants) may significantly reduce the rate of homocysteine methylation, leading to an elevation in homocysteine levels, which is a major risk factor for cardiovascular inflammation.

MTRR (5-methyleneterahydrofolate homocysteine methyltransferase reductase) — Involved in the recycling of homocysteine into methionine. MTRR methylates vitamin B-12, which is the major cofactor for this junction in the methylation cycle. MTRR works in concert with the MTHFR gene.

CBS (Cystathione beta synthase) — Involved in the conversion of homocysteine into cystathionine via transsulfuration. CBS is involved in Glutathione synthesis. Requires P5P (the active form of Vitamin B-6) for synthesis. Mutations are seen in abnormal detoxification. Glutathione is a critical antioxidant, capable of preventing oxidative, free radical damage to tissues.

NOS2 (Nitric oxide synthase 2) — Forms nitric oxide from L-arginine and L- citrulline. NADH, avin an biopterin (BH4), methylfolate are co-factors. NOS2 is the “inducible form”of the enzyme.

NOS3 (Nitric oxide synthase 3) — Forms nitric oxide from L-arginine and L- citrulline. NOS3 is expressed within the endothelium. NADH, avin an biopterin (BH4), methylfolate are co-factors.

PON1 (Paraoxonase) — Protein degrades organic chemicals and pesticides, such as parathion. Involved in the metabolism of statin drugs. PON1 enzymes prevent LDL oxidation and may be cardioprotective against atherosclerotic plaque. PON1 is also involved in the cardioprotective anti- oxidant activities of HDL.

PON2 (Paraoxonase) — PON2 enzymes prevent LDL oxidation, and may be cardioprotective against atherosclerotic plaque. PON2 may also enhance insulin utilization. PON2 is also involved in the cardioprotective anti-oxidant activities of HDL. PON2 may also enhance insulin utilization.

CoQ10A (Coenzyme Q10 A) — Essential for the function of Coenzyme Q10 within the mitochondria of cells. CoQ10 is a critical antioxidant with well-studied cardio-protective properties. Individuals taking statin medications are subject to depletion of CoQ10.

CoQ10B (Coenzyme Q10 B) — Essential for the function of Coenzyme Q10 within the mitochondria of cells. CoQ10 is a critical antioxidant with well-studied cardio-protective properties. Individuals taking statin medications are subject to depletion of CoQ10.

NDUFS7 (NADH dehydrogenase) — Involved in the mitochondrial electron transport chain. Involved in the transference of electrons from NADH to CoQ10.

IGF1R (insulin-like growth factor 1) — Has tyrosine kinase activity. Involved in antiapoptosis (anti-cell death). Mutations may be seen in insulin resistance &type 2 diabetes.

APOE (apolipoprotein) — Removes oxidized cholesterol. APOE 4/4 is associated with poor blood lipid profiles (in some, but not all people) when consuming high-fat diets. See APOE section for more details on your APOE genotype.

Immune-Related Genetics

Immune-Related genetics analyzes various genes related to immune system function. These are related to: immunoglobulins (IgA, IgG, IgE), cell signaling, cytokine activation, and the formation of various immune complexes.

Allergy & Mold

RS#	Call	Risk Allele	Gene	Variation	Result
rs2155219	GT	T	HLA		+/-
rs7775228	TT	C	HLA		-/-

HLA (Histocompatibility complex) — Present peptides derived from the endoplasmic reticulum

Celiac Disease

RS#	Call	Risk Allele	Gene	Variation	Result
rs2187668	CC	T	HLA DQA1		-/-
rs2858331	AG	G	HLA		+/-

HLA (Histocompatibility complex) — Present peptides derived from the endoplasmic reticulum.

HLA DQA1 (Histocombatibility complex) — Involved in antigen-presenting cells.

IgA

RS#	Call	Risk Allele	Gene	Variation	Result
rs9357155	GG	A	PSMB8 TAP1 TAP2		-/-
rs9275596	TT	C	MTC03P1		-/-
rs9275224	GG	A	HLA-DQA2		-/-
rs6677604	AG	A	CFH		+/-
rs9271366	AA	G	HLA		-/-
rs1990760	TT	C	IFIH1 (HLA)		-/-
rs3761847	AA	G	TRAF1		-/-
rs2229765	AA	A	IGF1R		+/+
rs4728142	AG	A	IRF5		+/-

TRAF 1 (TNF receptor associated 1) — Involved in the activation of the TNF (tumor necrosis factor) superfamily. Activates NF kappa B.

IRF5 (Interferon Regulatory Factor) — Involved in the formation of anti-viral cytokine interferon. May be involved in switching macrophages to increase or decrease interferon production. Mutations are seen in IBS, scleroderma.

IGF1R (insulin-like growth factor 1) — Has tyrosine kinase activity. Involved in antiapoptosis (anti-cell death). Mutations may be seen in insulin resistance & type 2 diabetes.

IFIH1 (Interferon-induced with helicase1) — Involved in nuclear & mitochondrial splicing. Associated with dermatological issues.

HLA DQA2 (Histocompatibility complex) — Peptide loading protein involved in CD4 T-cells.

CFH (complement Factor H) — Involved in the restriction of the innate immune defense against microbes.

HLA DQA2 (Major Histocompatibility complex, Class II DQA-alpha) – Involved in the CD4 T-cell antigen system via antigen-presenting cell pathways.

MTC03P1 — Data on this gene SNP is currently sparse. It is believed to play a role in Rheumatoid Arthritis, lupus, type 1 diabetes, multiple sclerosis. It has been studied in association with major histocompatibility genes HLA DQA.

PSMB8 (Proteasome Macropain subunit beta type 8) — Involved in cell apoptosis. May possess inflammatory responses.

IgE

RS#	Call	Risk Allele	Gene	Variation	Result
rs2240032	CT	T	RAD50		+/-
rs2040704	AG	G	RAD50		+/-
rs2251746	TT	C	FCER1A		-/-
rs33977706	AC	A	SOCS-1	-820G>T	+/-
rs2569191	TT	C	CD14		-/-
rs2814778	TT	C	DARC		-/-
rs1800925	CT	T	IL-13	C1112T	+/-

IL-13 (interleukin 13) — Anti-inflammatory cytokine derived from TH2 helper cells. Conditions associated with IL-13 mutations include: allergic asthma & rhinitis

DARC (Duffy blood group atypical chemokine receptor) - Functions as a chemokine

receptor for IL8, TARC, MCP1. Mutations may be implicated in genital herpes.

CD14 (CD14 molecule) — Cell surface bacterial-antigen expressed mostly on monocytes & macrophages.

SOCS1 (Suppressor of cytokine signaling 1) - Involved in negative feedback suppression of cytokine activation through the JAK/STAT3 pathway. May be involved in pituitary adenoma.

FCER1A (Fragment of IgE High Affinity) — Involved in allergic histamine response.

RAD-50 (DNA repair protein 50) — Involved in DNA repair and recombination, as well as telomere integrity. Involved in Nijmegen Syndrome

IgG

RS#	Call	Risk Allele	Gene	Variation	Result
rs7483	CT	T	GSTM3	V224I	+/-
rs1801274	AA	A	FCGR2A		+/+

FCGR2A (Fc Fragment of IgG, Low-Affinity IIa Receptor) — Cell surface receptor involved in operational phagocytosis of neutrophils & macrophages.

GSTM3 - (glutathione transferase - brain) — Involved in cellular detoxification of xenobiotics & carcinogens, believed to be expressed in brain tissue

Other Immune Factors

RS#	Call	Risk Allele	Gene	Variation	Result
rs2230926	TT	G	TNFAIP3		-/-
rs5029939	CC	G	TNFAIP3		-/-
rs1800629	GG	A	TNF-alpha	-308	-/-
rs2251746	TT	C	FCER1A		-/-
rs33977706	AC	A	SOCS-1	-820G>T	+/-
rs2569191	TT	C	CD14		-/-

IL-13 (interleukin 13) — Anti-inflammatory cytokine derived from TH2 helper cells. Conditions associated with IL-13 mutations include: allergic asthma & rhinitis

DARC (Duffy blood group atypical chemokine receptor) - Functions as a chemokine receptor for: IL8, TARC, MCP1. Mutations may be implicated in genital herpes.

CD14 (CD14 molecule) — Cell surface bacterial-antigen expressed mostly on monocytes & macrophages.

SOCS1 (Suppressor of cytokine signaling 1) - Involved in negative feedback suppression of cytokine activation through the JAK/STAT3 pathway. May be involved in pituitary adenoma.

FCER1A (Fragment of IgE High Affinity) — Involved in allergic histamine response.

TNF-alpha - Tumor necrosis factor-alpha is a potent TH1 cytokine operative in the inflammatory immune response. Carriers of the risk allele may experience increased risks of asthma, COPD, Crohn's disease, glaucoma, Grave's disease, heart disease, ischemic stroke, leprosy, lymphoma and liver disease (R). NOTE: This SNP has been the subject of a considerable number of studies in relation to many diseases.

TNFAIP3 - Tumor necrosis factor alpha induced protein 3 is a protein produced in response to the TNF-alpha cytokine. It has inhibitory effects on NF-kappa ß. The risk allele for rs5029939 is associated with autoimmune conditions, including systemic sclerosis (R), Sjogren's and Lupus complications (R). The risk allele for rs2230926 is associated with rheumatoid arthritis, Lupus and Sjrogren's (R).

TGFß

The TGFß section analyzes genes involved in TGFß signaling. The implications here apply to immune-related issues such as autoimmunity and inflammatory conditions.

RS#	Call	Risk Allele	Gene	Variation	Result
rs1143634	GG	A	IL1B		-/-
rs2104286	CT	T	IL2RA		+/-
rs3761548	T	T	FOXP3		+/-
rs1800469	GG	A	TGFß-1	H63D	-/-
rs1800471	CC	C	TGFß-1	C282Y	+/+

TGFß-1 - Transforming growth factor beta-1 is a growth factor and immune-modulating cytokine. rs1800471 risk factor is associated with hepatitis C viral infection (R), Crohn's Disease (R), myocardial infarction in men who have coronary heart disease (R), early-onset childhood asthma (R). rs1800469 is located in the promoter region of TGFß-1. The A risk allele generally increases the amount of TGFß-1 produced, and we interpret that as a greater overall risk than lower values of TGFß-1. This SNP is associated with a higher risk of COPD among smokers (R) and asthma (R).

FOXP3 - Forkhead box P3 is involved in the transcription of regulatory T-cells (TREGS), integral in the balance between the TH1 and TH2 immune systems, and for dampening excessive TH1 inflammatory activity. The risk allele for rs3761548 is associated with: allergic rhinitis (R). Rs3761549 is associated with: endometriosis and idiopathic infertility (R). FOXP3 is activated via TGFß signaling.

IL2Ra - Interleukin 2Ra is a receptor for the cytokine IL2. IL2 is a cytokine involved in T-regulatory cell differentiation and immunological tolerance. The risk allele is associated with autoimmune diseases, including Type 1 diabetes (R), multiple sclerosis (R), increased anti-nuclear antibodies (ANA) in females. Also associated with idiopathic juvenile arthritis (R).

IL1ß - Interleukin 1- beta Is a potent inflammatory cytokine, which promotes T-cell activation, including that of TH17. The risk allele for rs1143634 is associated with: larger waist circumference and obesity (R), alopecia (R), Alzheimer's risk (R), duodenal ulcers (R), Diabetic nephropathy (R), joint damage in rheumatoid arthritis (R), myasthenia gravis (R), inflammatory bowel disease (R), periodontitis (R), ulcerative colitis (R).

Individuals in this section with risk alleles may wish to consider TGFß-1 blood testing, especially if challenged with autoimmune conditions, Lyme disease, mold-related illness, and chronic inflammation.

Iron & Hemochromatosis-Related Genetics

The Iron and hemochromatosis genetics section analyzes genes related to iron activities, including those related to Iron stores (ferritin genes).

RS#	Call	Risk Allele	Gene	Variation	Result
rs242557	AA	A	MAPT		+/+
rs2071746	AT	T	HMOX1		+/-
rs235756	AG	A	BMP2		+/-
rs2230267	CT	C	FTL		+/-
rs1800730	AA	T	HFE	S65C	-/-
rs1799945	CG	G	HFE	H63D	+/-
rs1800562	GG	A	HFE	C282Y	-/-

HFE - Human hemochromatosis protein is associated with the activities of the storage form of iron known as Ferritin. The 3 SNPs listed are of greatest significance when assessing genetic hemochromatosis. The first 2 SNPs rs1800562 and rs1799945 are the most significant. Homozygosity (+/+) is associated with genetic hemochromatosis.

According to data, individuals with compound heterozygosity (+/- for each of the referenced SNPs) for the first 2 SNPs (rs1800562, rs1799945) may have mildly elevated iron stores, which in a very small percentage of cases leads to clinical symptoms of hemochromatosis.

According to a study on compound heterozygosity of HFE SNPs rs1800562, rs1799945, carriers of this combination are at low risk of hemochromatosis-related morbidity.

For male compound heterozygotes, mean iron indices do not change during middle age but

for female compound heterozygotes, menopause results in increased mean Ferritin levels. Although compound heterozygotes might maintain elevated iron indices during middle age, documented iron overload-related disease is rare (R).

According to a study from 2006, compound heterozygotes do tend to have higher iron indices but did not develop progressive clinical disease without comorbid factors such as obesity, steatosis, diabetes or excess alcohol consumption (R).

FTL - Ferritin light chain is a gene with little known function, yet the risk allele for rs2230267 is associated with elevated serum iron levels, transferrin saturation, ferritin and hereditary hemochromatosis prevalence (R). The FTL gene is associated

HAMP - Hepcidin antimicrobial peptide is a gene that regulates the activities of the protein

hepcidin. When iron levels increase in the blood, the liver produces hepcidin in order to reduce the absorption of iron in the intestines. rs10421768 is the SNP associated with the promoter region of the gene. The risk factor for rs10421768 may increase the risk of iron overload in beta-thalassemia (R) and may increase the susceptibility of extrapulmonary tuberculosis (R).

BMP2 - Bone morphogenetic protein 2 is a ligand of the TGFß family. The ligands of this gene bind to various TGFß receptors. rs235756 has been studied in association to hemochromatosis risk, with studies reporting divergent associations. A 2007 study found a significant association between rs235756 AA carriers and higher serum ferritin levels (R), while a 2015 study did not (R).

HMOX1 - Heme oxygenase-1 is the first step in the degradation of heme, the main constituent of hemoglobin. HMOX1 degrades heme into biliverdin. The HMOX1 risk allele for rs2071746 was studied in relation to Alzheimer's disease, along with an SNP of the MAPT gene, rs242557. The combined risk alleles were associated with a 6.65x increased incidence of Alzheimer's disease, compared to individuals without these combined risk alleles (R). Deficiencies of the HMOX1 protein are associated with COPD and pulmonary diseases.

MAPT - Microtubule-associated tau protein is a gene involved in the formation of tau protein. The hyperaccumulation of phosphorylated tau proteins results in neurofibrillary degeneration and tangles. Tau accumulation is a hallmark feature of neurodegenerative diseases such as Alzheimer's and Parkinson's diseases.

Individuals with genetic risk alleles for SNPs in this section should consider routine Ferritin blood testing, serum iron, and transferrin saturation levels to evaluate functional levels.

Methylation Genetics

Methylation refers to the process of adding a methyl group (CH3) to a substrate.Methylation is a central biochemical process responsible for:

- Removal of homocysteine (a potentially inflammatory protein)
- Glutathione formation (a critical antioxidant)
- Hormone and neurotransmitter synthesis and breakdown
- DNA/RNA synthesis and repair
- Nitric oxide formation
- Immune cell synthesis
- Biotransformation (“breaking down” of chemical, heavy metal and xenobiotic toxins)

Methylation - MAT1A

RS#	Call	Risk Allele	Gene	Variation	Result
rs2993763	GG	A	MAT1A		-/-
rs1819684	GG	T	MAT1A		-/-
rs11595587	GG	A	MAT1A		-/-
rs7081756	GT	T	MAT1A		+/-
rs1985908	AG	G	MAT1A		+/-
rs12242871	AG	A	MAT1A		+/-

MAT1A - Methionine adenosyl transferase is involved in the conversion of the amino acid methionine into S-adenosyl methionine, SAMe, which is the primary methyl donor. 70% of one-carbon methylation reactions involve SAMe as the cofactor, including reactions with most methyltransferases.

Methylation — ACAT (Acetyl coenzyme A transferase)

RS#	Call	Risk Allele	Gene	Variation	Result
rs3741049	GG	A	ACAT1-02		-/-

ACAT (Acetyl coenzyme A transferase) – Involved in the synthesis of Coenzyme A

Methylation — AHCY (Adenosyl homocysteinase)

RS#	Call	Risk Allele	Gene	Variation	Result
rs819171	TT	C	AHCY-19		-/-
rs819147	TT	C	AHCY-01		-/-

AHCY (Adenosyl homocysteinase) — Involved in homocysteine formation from L-methionine

Methylation — BHMT (Betaine homocysteine methyltransferase)

RS#	Call	Risk Allele	Gene	Variation	Result
rs3733890	GG	A	BHMT	R239Q	-/-
rs651852	CT	T	BHMT-08		+/-
rs567754	CT	T	BHMT-02		+/-
rs6875201	AA	G	BHMT		-/-

BHMT (Betaine homocysteine methyltransferase) — 'Back door re-methylation conversion' of homocysteine into methionine. Uses betaine as a cofactor.

Methylation — CBS (Cystathione beta synthase)

RS#	Call	Risk Allele	Gene	Variation	Result
rs4920037	GG	A	CBS	C19150T	-/-
rs2851391	CC	T	CBS	A13637G	-/-
rs1801181	AA	A	CBS	A360A	+/+
rs234706	GG	A	CBS	C699T	-/-

CBS (Cystathione beta synthase) — Involved in the conversion of homocysteine into cystathionine via transsulfuration. CBS is involved in Glutathione synthesis. Requires P5P (active form of Vitamin B-6) for synthesis. Mutations are seen in abnormal detoxification. Glutathione is a critical antioxidant, capable of preventing oxidative, free radical damage to tissues.

Methylation — COMT (Catechol-O-methyltransferase)

RS#	Call	Risk Allele	Gene	Variation	Result
rs6269	AA	G	COMT		-/-
rs4680	AA	A	COMT	V158M	+/+
rs4633	TT	T	COMT	H62H	+/+
rs769224	GG	A	COMT	-61 P199P	-/-

COMT (catechol-O-methyltransferase) — Involved in the breakdown of dopamine & norepinephrine. Mutations seen in behavioral disorders, and may involve abnormal concentrations of serotonin and norepinephrine.

Methylation — GAD1 (Glutamate decarboxylase)

RS#	Call	Risk Allele	Gene	Variation	Result
rs701492	CC	T	GAD1		-/-

rs3828275	CC	T	GAD1	-/-
rs10432420	GG	A	GAD1	-/-
rs3791878	GT	T	GAD1	+/-
rs12185692	CC	A	GAD1	-/-
rs3791850	GG	A	GAD1	-/-
rs3791851	TT	C	GAD1	-/-
rs2058725	TT	C	GAD1	-/-
rs769407	GG	C	GAD1	-/-
rs2241165	TT	C	GAD1	-/-
rs3749034	GG	A	GAD1	-/-

GAD1 (Glutamate decarboxylase) — Involved in conversion of glutamate to GABA. Mutations are seen in glutamate excitotoxicity, GABA deficiency. Vitamin B-6 (P5P) is a cofactor.

Methylation — MAO-A (Monamine oxidase)

RS#	Call	Risk Allele	Gene	Variation	Result
rs6323	T	T	MAO A	R297R	+/-

MAO-A (Monamine oxidase) — Involved in the breakdown of serotonin.Mutations seen in mood/behavior issues. May lead to abnormal serotonin.

Methylation — Misc

RS#	Call	Risk Allele	Gene	Variation	Result
rs1544410	CC	T	VDR	Bsm	-/-
rs1801198	CC	G	TCN2	C766G	-/-
rs526934	AA	G	TCN1		-/-
rs55776826	CC	T	GAMT		-/-
rs17851582	GG	A	GAMT		-/-
rs1050829	T	C	G6PD		-/-
rs1050828	C	T	G6PD		-/-
rs699	AG	G	AGT	M235T (C4072T)	+/-
rs4343	AG	G	ACE	Del16	+/-
rs6495446	CC	C	MTHFS		+/+
rs803422	GG	A	MTHFD1L		-/-

rs6922269	GG	A	MTHFD1L		-/-
rs17349743	CT	C	MTHFD1L		+/-
rs11754661	GG	A	MTHFD1L		-/-
rs2236225	AG	A	MTHFD1	G1958A	+/-
rs1076991	CT	C	MTHFD1	C105T	+/-
rs1643649	CT	C	DHFR		+/-
rs7925545	AA	G	FOLR3		-/-
rs651933	GG	A	FOLR2		-/-
rs2071010	GG	A	FOLR1		-/-
rs3918188	AC	A	NOS3		+/-
rs1800779	AG	G	NOS3		+/-
rs1800783	AT	A	NOS3		+/-
rs2248814	GG	A	NOS2		-/-
rs2274894	GG	T	NOS2		-/-
rs2297518	AG	A	NOS2		+/-
rs3741775	CC	C	DAO		+/+
rs2070586	GG	A	DAO		-/-
rs34095989	GG	A	SHMT2		-/-
rs7946	TT	C	PEMT		-/-
rs4646406	AT	A	PEMT		+/-
rs4244593	GT	T	PEMT		+/-
rs558660	GG	A	GIF (TCN3)		-/-
rs602662	AG	A	FUT2		+/-
rs601338	AG	A	FUT2		+/-
rs492602	AG	G	FUT2		+/-

FOLR 1,2,3 (Folate receptor 1,2,3) — Involved in the transport of 5-methylfolate into cells. Mutations are seen in cerebral neuro-degeneration. Mutations are seen in neural tube defects & RA.

DHFR (dihydrofolate reductase) - Folate derivative involved in purine synthesis.

MTHFD1 (methylene tetrahydrofolate dehydrogenase 1) — Involved in the conversion of methylated folate derivatives into purine and thymidilate synthesis. These processes are

important for DNA synthesis and repair.

SHMT (serine hydroxymethyltransferase) — Involved in purine synthesis via folate derivatives. Mutations may involve abnormal iron metabolism & predisposition to GI pathogens

MTHFS (methylene tetrahydrofolate cyclo ligase) — Folate derivative involved in the formation of purines, thymidine, and amino acids.

NOS2 (Nitric oxide synthase 2) — Forms nitric oxide from L-arginine and L- citrulline. NADH, avin an biopterin (BH4), methylfolate are co-factors. NOS2 is the “inducible form” of the enzyme.

NOS3 (Nitric oxide synthase 3) — Forms nitric oxide from L-arginine and L- citrulline. NOS3 is expressed within the endothelium. NADH, avin an biopterin (BH4), methylfolate are co-factors.

ACE (angiotensin 1 converting enzyme) — Involved in blood pressure regulation through the angiotensin system.

AGT (Angiotensinogen) — Involved in blood pressure regulation. Mutations are seen in hypertension.

DAO (di-amino oxidase) — Enzyme involved in the degradation of histamine. Involved in dopamine synthesis. Regulates L-Serine in the brain. Mutations are seen in schizophrenia & bi-polar. Histamine is an immune compound as well as a neurotransmitter.

FUT2 (Fucosyltransferase 2) — Involved in H antigen formation through oligosaccharide FuC alpha. Associated with intestinal flora imbalance & Crohn’s disease. Mutations in FUT2 may predispose towards low concentrations of bifidobacterium. FUT2 may also be involved in Vitamin B-12 levels.

G6PD (Glucose-5-phosphate dehydrogenase) - G6PD is critical for proper glucose synthesis and utilization by converting glucose into ribose-5-phosphate, which is used for nucleotide synthesis. As a result of this reaction, NADPH is formed. NADPH is a critical reducing agent, and antioxidant. G6PD is also critical as an antioxidant of red blood cells. Mutations are seen in hemolytic anemia.

GAMT (Guaidinoacetate n-methyltransferase) — Creatine formation from s- adenosyl methionine.

GIF (Gastric intrinsic factor) - Involved in the formation of intrinsic factor for B-12 utilization. Intrinsic factor is produced by the parietal cells of the stomach.

PEMT (phosphatidylethanolamine methyltransferase) — Involved in the conversion of the phospholipid ethanolamine into phosphatidylcholine. Phospholipids are components of cellular membranes, and facilitate vital functions in the brain, liver, intestines and nervous

system.

TCN1 (Transcobalamin I) — Involved in the transport of cobalamin into cells. May indicate B-12 deficiency.

TCN2 (Transcobalamin II) — Involved in the transport of cobalamin into cells. May indicate B-12 deficiency.

VDR BSM (Vitamin D Receptor) — Involved in the nuclear reception of Vitamin D.

Methylation — MTHFR, MTR, MTRR, & SLC19A1

RS#	Call	Risk Allele	Gene	Variation	Result
rs1051266	CT	T	SLC19a1	G80A	+/-
rs9332	GG	A	MTRR		-/-
rs3776467	AA	G	MTRR		-/-
rs1532268	CC	T	MTRR		-/-
rs162036	AA	G	MTRR	K350A	-/-
rs1805087	AG	G	MTR	A2756G	+/-
rs2274976	CC	T	MTHFR	G1793A (R594Q)	-/-
rs2066470	GG	A	MTHFR 03	P39P	-/-
rs17367504	AA	G	MTHFR	A1572G	-/-
rs1802059	GG	A	MTRR-11	A664A	-/-
rs1801394	GG	G	MTRR	A66G	+/+
rs1801131	TT	G	MTHFR	A1298C	-/-
rs1801133	GG	A	MTHFR	C677T	-/-

MTHFR (Methylene tetrahydrofolate reductase) — Involved in the formation of 5-methyl folate. The active, methylated folate is central to methylation cycle function, and the “remethylation” of homocysteine. Mutations in MTHFR genes (especially C677T and A1298C variants) may significantly reduce the rate of homocysteine methylation, leading to an elevation in homocysteine levels, which is a major risk factor for cardiovascular inflammation. Additionally, methylfolate is an essential substrate for neurotransmitter synthesis as well as DNA synthesis and repair.

MTR (5-Methyltetrahydrofolate homocysteine methyltransferase) - Functions as an intermediary to transfer of methyl groups from MTHFR to MTRR for the remethylation of homocysteine. Uses B-12 as cofactor.

MTRR (5-methyleneterahydrofolate homocysteine methyltransferase reductase) —

Involved in the recycling of homocysteine into methionine. MTRR methylates vitamin B-12, which is the major cofactor for this junction in the methylation cycle. MTRR works in concert with the MTHFR gene.

SLC19A1 is the folate transporter protein. The TT genotype is associated with lower plasma folate levels (R).

Mitochondrial Genetics

Mitochondrial genetics analyzes various genes related to mitochondrial function. It is believed that mitochondrial genetics evolved differently than nuclear genetics. The mitochondria are the “energy-burning furnaces” in our cells. Our Mitochondria generate biological energy (ATP) from nutrients, and use critical antioxidants to protect from excess free radicals and toxicity.

RS#	Call	Risk Allele	Gene	Variation	Result
rs11648723	GG	T	UQCRC2		-/-
rs4850	GG	A	UQCRC2		-/-
rs1051806	CT	T	NDUFS8		+/-
rs2075626	CC	C	NDUFS8		+/+
rs999571	AG	A	NDUFS8		+/-
rs4147730	GG	A	NDUFS3		-/-
rs4626565	CT	C	COX6C		+/-
rs8042694	AA	G	COX5A		-/-
rs1244414	CC	T	ATP5c1		-/-
rs36089250	TT	C	ATP5g3		-/-
rs809359	AG	G	NDUFS7		+/-
rs7258846	GT	T	NDUFS7		+/-
rs1142530	CT	T	NDUFS7		+/-
rs2332496	AG	A	NDUFS7		+/-

ATP5G3 (ATP synthase, H+ transporting mitochondrial Fo complex) - ATP synthesis. Mutations may be seen in urea cycle dysfunction.

ATP5C1 (ATP synthase, H+ transporting mitochondrial F1 complex) - ATP synthesis. Mutations may be seen in Huntington’s disease.

COX5A (Cytrochrome C oxidase 5A) — Transfers electrons from cytochrome C to oxygen in the respiratory chain.

COX6C (Cytochrome C oxidase 6C) — Transfers electrons from cytochrome C to oxygen in the respiratory chain.

NDUFS3 (NADH dehydrogenase) — Involved in the electron transport chain. NADH transferring of electrons to CoQ10.

NDUFS7 (NADH dehydrogenase) — Involved in the mitochondrial electron transport chain. Involved in the transference of electrons from NADH to CoQ10.

NDUFS8 (NADH dehydrogenase) — Involved in the electron transport chain. NADH transferring of electrons to CoQ10.

UQCRC2 (Ubiquinol cytochrome C reductase core) — CoQ10 cytochrome C assembly system in the respiratory chain of the mitochondria

Oxalate-Related Genes

Oxalate metabolism genetics is potentially relevant to identify predisposing genetic factors to the disturbances in oxalate metabolism, including related issues such as hyperoxaluria, kidney stone formation, calcium-oxalate pain syndromes, and dietary oxalate and/or sulfur sensitivities.

RS#	Call	Risk Allele	Gene	Variation	Result
rs807669	CT	T	SLC25a1		+/-
rs2297644	TT	C	HOGA1		-/-
rs35382133	TT	T	SPP1		+/+
rs1126616	CT	T	SPP1	Ala250	+/-
rs6840362	CC	T	SPP1		-/-
rs4754	CT	C	SPP1		+/-
rs11728697	CT	C	SPP1		+/-
rs2853744	GG	G	SPP1		+/+
rs2768659	AG	G	GRHPR		+/-

GRHPR - Glyoxylate hydroxypyruvate converts potentially harmful glyoxylate into inert glycolate. This enzyme is also involved in the conversion of hydroxypyruvate into D-glycerate. In the absence of the enzyme glyoxylate-aminotransferase, glyoxylate is converted into oxalic acid.

SPP1 - Osteopontin is a gene involved in calcium metabolism and in the formation of calcium-oxalate crystals. Additionally, osteopontin is reportedly a TH1 cytokine. Research has found the GG genotype of rs2853744 is associated with risk of calcium oxalate urolithiasis (R). Additionally, rs28357094 TT genotype and rs2728127 GG genotype of the SPP1 gene were found to be predisposing. The TT genotype for rs1126616 is significantly associated with urinary stone formation, with T-allele carriers having a 1.8-fold increase in urinary stone formation compared to C-allele carriers. Heterozygotes (CT) were also found to be associated with a higher urinary stone formation risk (R). Additionally, the T risk allele for rs1126616 is associated with lupus (R). C allele of rs4754, rs11728697 and rs11730582 are associated with risk of sarcoidosis (R).

HOG1A - 4-hydroxy-2-oxoglutaric aldoase releases glyoxylate and pyruvate via the hydroxyproline pathway. rs2297644 of the HOGA1 gene is associated with serum Glutamine levels, and the ratio of Glutamine to Histidine (R). rs807669 of the SLC25a1 gene is associated with serum levels of citrate (R). Citrate is known to inhibit oxalate. T is the minor allele of rs807669 (R).

Individuals with risk alleles in this section may wish to monitor urinary oxalate activity

through urinary organic acids testing.

SHBG: Sex Hormone Binding Globulin

SHBG analyzes various genes related to sex hormone binding globulin.

RS#	Call	Risk Allele	Gene	Variation	Result
rs727428	CT	C	SHBG		+/-
rs1799941	AG	A	SHBG		+/-

SHBG - Sex hormone binding globulin is a protein which binds to and makes inactive sex hormones testosterone and estrogen. Rs179941 is associated with levels of SHBG (sex hormone binding globulin) (R). The genotype AA for Rs179941 is associated with 0.4 standard deviations higher SHBG levels. While there may be some benefit to higher SHBG levels, we interpret “A” as the risk allele for Rs179941.

Rs727428 is associated with SHBG levels. In a study of 758 females studying the association between various SHBG SNPs and obesity and insulin resistance, the AA genotype of Rs727428 was shown to have SHBG levels 27% lower than the CC genotype, and the CT genotype was shown to have a 13% lower SHBG levels compared to the CC genotype (R).

Individuals with risk alleles in this section may wish to test blood levels of SHBG.

Thyroid

Thyroid Factor Genetics analyzes various genes involved in thyroid function & health, as well as those associated with autoimmune thyroid conditions.

RS#	Call	Risk Allele	Gene	Variation	Result
rs10984009	GG	A	FOXE1		-/-
rs1867277	GG	A	FOXE1		-/-
rs231775	AA	G	CTLA4		-/-

CTLA4 (Cytotoxic T-lymphocyte-associated protein 4) — Transmits inhibitory signal to T-cells. Mutations seen in Graves disease, Hashimoto's & Type 1 Diabetes.

FOXE1 (Forkhead box E1; thyroid transcription factor) — Involved in the formation of congenital hypothyroidism.

Vaccine Adverse Events

MMR Vaccine Adverse Events

Section Description: This section is based upon a study which found genetic variants associated with general & MMR-related febrile seizures.

RS#	Call	Risk Allele	Gene	Variation	Result
rs273259	GG	A	IFI44L	Missense variant	-/-
rs6432860	AG	G	SCN1a		+/-

Source: Feenstra B, et al. Common variants associated with general and MMR vaccine-related febrile seizures. Nat Genet. 2014 Dec;46(12):1274-82. doi: 10.1038/ng.3129. Epub 2014 Oct 26

SCN1A - Voltage-dependent sodium channel gene with risk alleles associated with epilepsy and febrile seizures.

SCN2a - Voltage-gated sodium channel gene with risk alleles associated with autism spectrum and seizure disorders.

IFI44L - Interferon-inducing gene with antiviral actions.

TMEM16 - Also known as anoctamins, this gene is involved in calcium and chloride ion channel activities, neuronal excitation and phospholipid scrambling.

rs11105468 - Intergenic gene associated with magnesium levels.

Smallpox Vaccine Adverse Events

This section is based upon literature that showed that certain SNPs have an association with vaccine-related adverse events following smallpox vaccination. Future research is needed to study the relationship between these SNPs and adverse events with other vaccines.

RS#	Call	Risk Allele	Gene	Variation	Result
rs2243290	AC	A	IL4		+/-
rs2243268	AC	C	IL4		+/-
rs2070874	CT	T	IL4		+/-
rs839	CT	T	IRF1		+/-
rs9282763	CT	C	IRF1		+/-
rs1801133	GG	A	MTHFR	C677T	-/-

Vitamin A Metabolism

Vitamin A Metabolism genetics analyzes various genes involved in the conversion of beta carotene into Vitamin A (retinol).

RS#	Call	Risk Allele	Gene	Variation	Result
rs2241057	AG	A	CYP26B1		+/-
rs6420424	AA	A	BCMO1	C754T	+/+
rs11645428	GG	g	BCMO1		-/-
rs6564851	GG	G	BCMO1		+/+
rs7501331	CT	T	BCMO1	A379V	+/-
rs12934922	AA	T	BCMO1	R267S	-/-

BCMO1 - Beta carotene monooxygenase is essential in the conversion of ß-carotene into Vitamin A. Contrary to government-sponsored nutrition food labels, ß-carotene found in plant foods is not synonymous with Vitamin A. Variations of the BCMO1 gene should be strongly considered when recommending vegetarian or vegan-based diets, especially if carriers feature reduced capacity to form Vitamin A from ß-carotene.

Homozygous carriers of the G risk allele for rs11645428 have shown a 51% decrease in the conversion efficiency of ß-carotene into Vitamin A . Homozygous carriers of the A risk allele for rs6420424 have shown a 59% decrease in the conversion efficiency of ß-carotene into Vitamin A. Homozygous carriers of rs6564851 also show reduced metabolism of ß-carotene into Vitamin A (R).

Combined homozygotes for rs12934922 and rs7501331 have shown a reduced ß-carotene to Vitamin A conversion by 57%. Heterozygotes for the SNP's also have shown reduced conversion into Vitamin A (R).

CYP26B1 is a cytochrome enzyme involved in the catabolism of retinoic acid. The A risk allele for rs2241057 is associated with an increased breakdown of retinoic acid, and is also associated with Crohn's disease (R).

Individuals with risk alleles in this section may wish to test plasma levels of Vitamin A, especially if on vegan or vegetarian diets.

Vitamin D Metabolism

Vitamin D metabolism analyzes SNPs related to vitamin D activities.

RS#	Call	Risk Allele	Gene	Variation	Result
rs2228570	AA	G	VDR	FOK1	-/-
rs3829251	GG	A	NADSYN1		-/-
rs2060793	AG	A	CYP2R1		+/-
rs2282679	TT	G	VDBP		-/-
rs7041	CC	A	VDBP		-/-
rs731236	AA	G	VDR	TaQ1	-/-
rs1544410	CC	T	VDR	Bsm	-/-

VDR - Is the Vitamin D receptor. VDR is activated by Calcitriol, the active seco-steroid hormone form of Vitamin D. VDR is a nuclear receptor, with numerous post-translational effects, including immunological, calcium-related and hormone-related activations.

VDBP - Vitamin D binding protein is also known as “GC Globulin” is a transport protein for many or most forms of Vitamin D in circulation including 25OHD and 1,25 DiHydroxy (Calcitriol). The VDBP is also known as a GC-MAF (macrophage activating factor), which has been studied in relation to cancer treatments.

The A risk allele for rs7041 is associated with greater risk of depression when consuming a higher protein/low fat diet (R). Pregnant AA homozygotes for rs7041 showed significantly lower circulating levels of 25OHD, VDBP, and lower placental levels of 25OHD, while higher “free” levels of 25OHD (R).

The C risk allele for rs2282679 is associated with lower 25OH D levels (R).

CYP2R1 - This cytochrome enzyme is involved in the conversion of Vitamin D3 into 25OH Vitamin D. The risk allele for rs2060793 is associated with lower levels of 25OHD due to a reduction in this conversion (R).

NADSYN1 - Nicotinamide adenine dinucleotide synthetase is involved in the final step conversion of NaAD into NAD. rs3829251 along with SNP’s rs2282679 and rs6599638 account for a 2.8% of the variation of circulating 25OH D levels (R).

Individuals with risk alleles in this section may wish to monitor blood tests for both forms of Vitamin D: 25OHD and 1,25 dihydroxy vitamin D (calcitriol).

Support

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