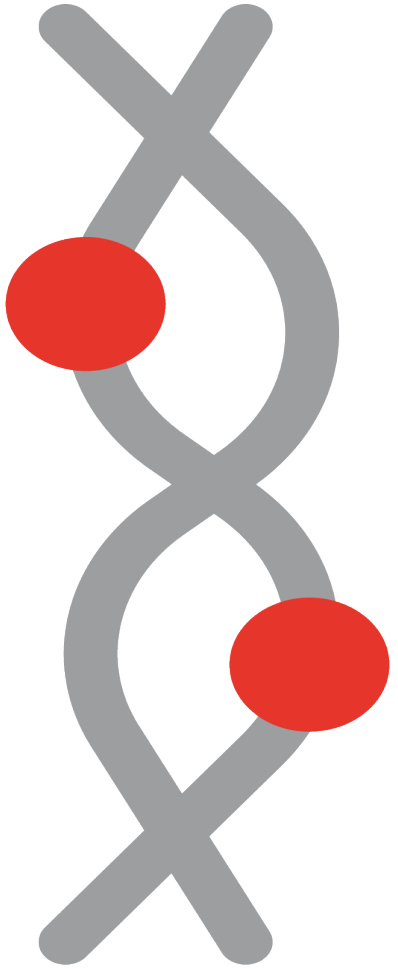
LIFE EXTENSION®

The Science of a Healthier Life™



Gene Comprehensive Nutrigenomic Report

Accession Number: ##########
Specimen Collected: ##/##/####
Specimen Received: ##/##/####
Report Generated: October 17, 2024
Specimen Type: Buccal Swab
Provider: ######## ########
Patient Name: ###### ######
Patient DOB: ##/##/####
Patient Gender: Female

Do not make any decisions about your health solely based on the information contained in this report. Always consult with a licensed and experienced health practitioner when you receive this report.

Fagron Genomics US | 844-258-5564 | FagronGenomicsUS.com
Lab | 807 Las Cimas Pkwy, Suite 145 | Austin, TX 78746
Laboratory Director: James W. Jacobson, Ph.D

– 32 – Female

(-/-) Normal Risk | (-/+) Medium Risk | (+/+) High Risk

rsID	Gene	Genetic Result	This column contains the targeted ingredients to support healthy gene activity of the specific genes listed.	Lifestyle Recommendations	Laboratory Recommendations
INFLAMMATORY					
rs2250656	C3	T/C (+/-)	Anti-Inflammatory Therapy: Curcumin, Omega-3 Fatty Acids, Resveratrol, Quercetin, Low Dose Naltrexone (LDN), CBD Oil	Consider Anti-inflammatory Diet and Lifestyle	**General Inflammatory Markers:** Serum High Sensitivity C-Reactive Protein, Serum Iron and Ferritin, Erythrocyte Sedimentation Rate, Serum Complement C3, Serum Interleukin 6 Lymphocyte Profile AND/OR Antibody Testing **Additional Options:** Adrenal Stress Profile, Sex Hormone Panel, Full Thyroid Panel, Food Allergy Panel, Comprehensive Micronutrient Testing, Microbial Titer (Candida, Epstein-Barr Virus, etc.), Toxic Metal Testing, Environmental Allergy Testing
rs2569190	CD14	A/G (+/-)			
rs2069812	IL5	A/G (+/-)			
rs1800925	IL13	C/C (-/-)			
rs10181656	STAT4	C/G (+/-)			
rs1800795	IL6	C/G (+/-)			
rs1800629	TNF	G/G (-/-)			
rs231775	CTLA4	A/A (-/-)			
rs4795067	NOS2	A/G (+/-)	Inducible Nitric Oxide Synthase (iNOS) Activity, Anti-Infectives, Beta Glucans	Increased iNOS Activity May Promote Higher Levels of Inflammation	

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EXTERNAL INFLAMMATORY					
Histamine Sensitivity					
rs10156191	AOC1	C/C (-/-)	Poor Ability to Break Down External Histamine		
Gluten Sensitivity					
rs2187668	HLA DQA1	C/T (+/-)	High Risk of Gluten and Casein Sensitivity, Broad Spectrum Enzyme	Consider Gluten and Dairy Avoidance	Food Allergy Panel if GI Inflammation Is Present
rs7454108	HLA DQB1	T/T (-/-)			
Microbiome Stability					
rs492602	FUT2	A/G (+/-)	Prebiotics and Probiotics Needed	Consider Consumption of Prebiotic and Probiotic Foods	
Vitamin D					
rs2228570	VDR	A/A (+/+)	Vitamin D, Vitamin K		Consider Checking Vitamin D Levels OR Comprehensive Micronutrient Testing
AUTOPHAGY					
rs510432	ATG5	T/T (-/-)	Curcumin, Lithium Orotate, D-Chiro-Inositol, Catechins, Resveratrol, Caffeine, 12 Hour Fasting	May Have Reduced Blood Sugar Control Intermittent Fasting (12-15 Hours) Exercise Regularly	Routine Blood Sugar, Insulin, and HbA1c
rs26538	ATG12	C/T (+/-)			
rs10210302	ATG16L1	C/T (+/-)			

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MITOCHONDRIA					
rs1467568	SIRT1	A/G (+/-)	Pterostilbene, Resveratrol, Quercetin, NAD+, Coenzyme Q10, Pyrroloquinoline Quinone (PQQ), L-Carnitine, Ornithine, Magnesium, Calcium	Exercise Regularly Caloric Restriction	Organic Acid Testing
rs8192678	PPARGC1A	C/C (-/-)			
rs1937	TFAM	G/G (+/+)			
CoQ10					
rs1800566	NQO1	G/G (-/-)	Coenzyme Q10, Pyrroloquinoline Quinone (PQQ), Riboflavin		
Oxidative Stress					
rs6721961	NFE2L2	G/G (-/-)	Pterostilbene, Green Tea (Epigallocatechin Gallate), Turmeric, Sulforaphane, Endurance Exercise	Consume Antioxidant Rich Diet	
rs4880	SOD2	A/G (+/-)	High Dose Antioxidants, Curcumin, Sulforaphane, Vitamin C		
Antioxidants					
rs33972313	SLC23A1	C/C (-/-)	High Dose Vitamin C		
rs6994076	TTPA	A/A (-/-)	Vitamin E		

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METHYLATION					
Folate Metabolism					
rs1051266	SLC19A1	T/C (+/-)	Methyltetrahydrofolate (B9), Riboflavin (B2), Niacinamide (B3)		Complete Blood Count Serum and RBC Folate
rs2071010	FOLR1	G/G (-/-)			
rs70991108	DHFR	DEL/DEL (-/-)			
rs1076991	MTHFD1	C/T (+/-)			
rs1801133	MTHFR C677T	G/A (+/-)			
rs1801131	MTHFR A1298C	T/T (-/-)			
Vitamin B12 Metabolism					
rs526934	TCN1	A/A (-/-)	Methylcobalamin, Adenosylcobalamin		Serum Vitamin B12
rs1801222	CUBN	A/G (+/-)			
rs1801198	TCN2	C/C (-/-)			
rs1801394	MTRR	A/A (-/-)	Methylcobalamin (B12)		

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HOMOCYSTEINE METABOLISM					
Remethylation					
rs1805087	MTR	A/A (+/+)	Methyltetrahydrofolate, Methylcobalamin, Methionine	Avoid Smoking and Heavy Alcohol Consumption	Plasma Methylation Profile OR Plasma Homocysteine Serum Vitamin B12
rs3733890	BHMT	A/G (+/-)	Choline, Trimethylglycine (Betaine)		Plasma Methylation Profile OR Plasma Homocysteine
Catabolism					
rs234706	CBS	G/A (+/-)	Methyltetrahydrofolate, Methylcobalamin, Pyridoxal 5'-Phosphate (B6), Choline, Trimethylglycine, Serine, N-Acetyl Cysteine	Avoid Smoking and Heavy Alcohol Consumption Consider Anti-Inflammatory Diet and Lifestyle	Plasma Methylation Profile OR Plasma Homocysteine
rs1021737	CTH	G/T (+/-)	N-Acetyl Cysteine, Glutathione, Pyridoxal 5'-Phosphate	Avoid Smoking and Heavy Alcohol Consumption Avoid Herbicides and Pesticides	

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rsID	Gene	Genetic Result	This column contains the targeted ingredients to support healthy gene activity of the specific genes listed.	Lifestyle Recommendations	Laboratory Recommendations
DETOXIFICATION					
rs8190955	GSR	G/G (-/-)	Riboflavin, Reduced Glutathione		
rs17883901	GCLC	G/G (-/-)	Glutathione		
rs1695	GSTP1	A/G (+/-)	N-Acetyl Cysteine (NAC), Glutathione	Avoid Herbicides and Pesticides Consider Pre-Anesthesia Glutathione	Whole Blood Glutathione
rs1801280	NAT2	C/C (+/+)	Silymarin, Alpha Lipoic Acid (ALA), P-5-P, Catechins	Avoid Industrial Carcinogens	

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NEUROTRANSMITTER					
rs4680	COMT	A/G (+/-)	Riboflavin (B2), Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Methionine, SAMe, Inositol, L-Methionine	High Risk of Depression/Anxiety	Neurotransmitter Metabolite Testing Consider PGx Testing
rs6323	MAOA	T/T (-/-)	Riboflavin (B2), Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Methionine, SAMe, Inositol, L-Methionine		
rs1799836	MAOB	T/C (+/-)			
rs3828275	GAD1	C/C (-/-)	Prescription Amantadine, Ketamine, Glycine, N-Acetyl-Cysteine (NAC), Zinc, Magnesium, Oxaloacetate, Elderberry, L-Theanine, Melatonin		
rs769407	GAD1	C/G (+/-)			
rs2274924	TRPM6	T/T (-/-)	Magnesium		

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HEALTH PRECAUTIONS					
Thyroid Health					
rs4704397	PDE8B	A/G (+/-)	Iodine, Selenium, Increased Risk of Hypothyroidism		Thyroid Panel Urinary Iodine OR Comprehesive Micronuritent/Mineral Analysis
Estrogen Conversion					
rs4646	CYP19A1	C/C (+/+)	High Activity of Aromatase, Higher Risk of Excess Estrogen Production	Testosterone Therapy May Produce High Levels of Estrogen	Sex Hormones and Metabolites Panel including Progesterone, Testosterone, and Estrogen
Hypertension Risk					
rs4343	ACE	A/G (+/-)	Increased Risk of Salt Retention and Hypertension	Increased Risk of Hypertension and Preeclampsia Salt Restriction, Especially after Age 40	
Caffeine Sensitivity					
rs762551	CYP1A2	A/A (-/-)	Caffeine Metabolism: Slow Metabolizer (CC genotype), Intermediate Metabolizer (CA genotype), Rapid Metabolizer (AA genotype)		
Clot Risk					
rs6025	F5	C/C (-/-)	Increased Risk of Blood Clots	Be Cautious with (or Avoid) the Use of Estrogen and Vitamin K Supplementation as It May Lead to Increased Risk of Blood Clots	Prothrombin Time
rs3211719	F10	G/G (+/+)			

Summary for Optimal Wellness Genetic Insights Panel

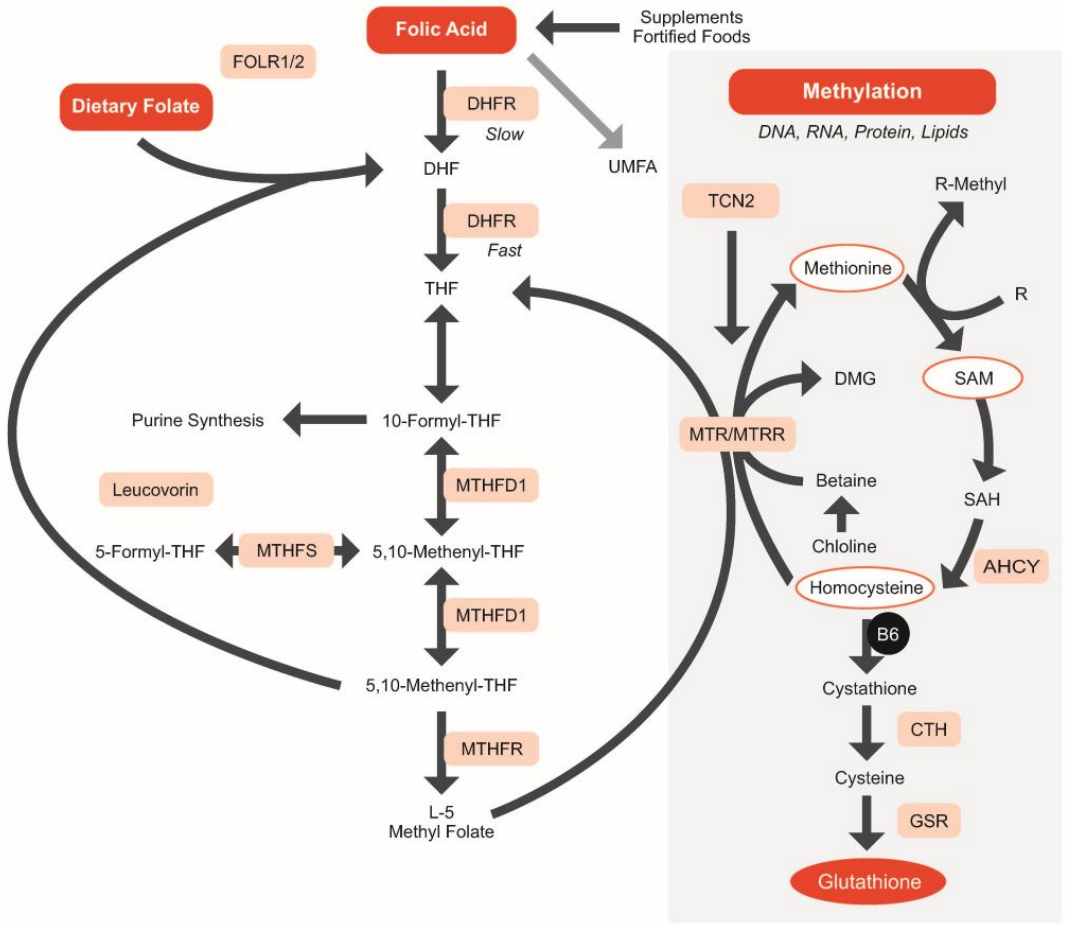
Lifestyle Recommendations

- Consider Anti-inflammatory Diet and Lifestyle
- Increased iNOS Activity May Promote Higher Levels of Inflammation
- Consider Gluten and Dairy Avoidance
- Consider Consumption of Prebiotic and Probiotic Foods
- May Have Reduced Blood Sugar Control
- Intermittent Fasting (12-15 Hours)
- Exercise Regularly
- Caloric Restriction
- Consume Antioxidant Rich Diet
- Avoid Smoking and Heavy Alcohol Consumption
- Consider Anti-Inflammatory Diet and Lifestyle
- Avoid Herbicides and Pesticides
- Consider Pre-Anesthesia Glutathione
- Avoid Industrial Carcinogens
- High Risk of Depression/Anxiety
- Testosterone Therapy May Produce High Levels of Estrogen
- Increased Risk of Hypertension and Preeclampsia
- Salt Restriction, Especially after Age 40
- Be Cautious with (or Avoid) the Use of Estrogen and Vitamin K Supplementation as It May Lead to Increased Risk of Blood Clots

Laboratory Recommendations

- General Inflammatory Markers: Serum High Sensitivity C-Reactive Protein, Serum Iron and Ferritin, Erythrocyte Sedimentation Rate, Serum Complement C3, Serum Interleukin 6
- Lymphocyte Profile AND/OR Antibody Testing
- Additional Options: Adrenal Stress Profile, Sex Hormone Panel, Full Thyroid Panel, Food Allergy Panel, Comprehensive Micronutrient Testing, Microbial Titer (Candida, Epstein-Barr Virus, etc.), Toxic Metal Testing, Environmental Allergy Testing
- Food Allergy Panel if GI Inflammation Is Present
- Consider Checking Vitamin D Levels OR Comprehensive Micronutrient Testing
- Routine Blood Sugar, Insulin, and HbA1c
- Organic Acid Testing
- Complete Blood Count
- Serum and RBC Folate
- Serum Vitamin B12
- Plasma Methylation Profile OR Plasma Homocysteine
- Whole Blood Glutathione
- Neurotransmitter Metabolite Testing
- Consider PGx Testing
- Thyroid Panel
- Urinary Iodine OR Comprehesive Micronuritent/Mineral Analysis
- Sex Hormones and Metabolites Panel including Progesterone, Testosterone, and Estrogen
- Prothrombin Time

METHYLATION



Methylation

- Involves the addition of a methyl group (CH3)
- Regulates gene expression and repression
- Reduces or removes toxins that eliminate essential nutrients
- Provides nutrients needed for processes such as detoxification, immune regulation, gut health

Methionine

- Used in protein formation and stabilization
- Elevated levels are associated with risk for coronary heart disease, stroke & neurological diseases

Glutathione

- Important for chemical detoxification & proper mitochondrial functioning
- Genes relevant for production include: AHCY, CTH, CGTP1, GSTM1, GSTM3, GSR, MTRR & MTR

5-Methyl Folate

- Important for dopamine and serotonin formation, detoxification and mitochondrial strength
- Genes relevant for production include: DHFR, FOLR1/2, MTHFD1, MTHFR, MTHFS

Homocysteine

- Elevated levels are associated with risk for coronary heart disease, stroke, neurological diseases
- Variants in the methylation pathway can be associated with increased/decreased levels

FOLATE

FOOD SOURCES


Eggs


Citrus Fruits

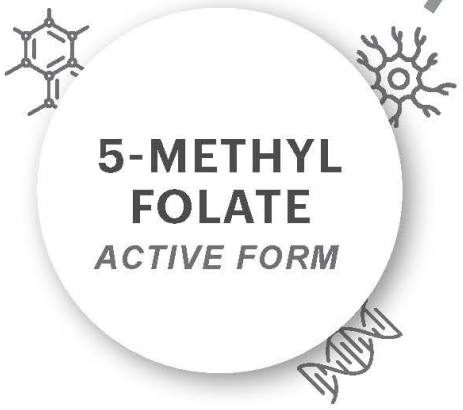

Leafy Greens


Legumes


Broccoli


Brussel Sprouts


Breads, Cereal, Pastas, Rice



FUNCTIONS (OR BENEFITS AS YOU AGE)

- Maintains structure & function of proteins
- Maintains structure & function of DNA
- Facilitates DNA replication, neurotransmitter production & detoxification

DEFICIENCY CAUSES

- Neural tube defects
- Cardiovascular disease
- Memory problems
- Depression
- Insomnia
- Irritability

VITAMIN B12

FOOD SOURCES


Eggs


Seafood – clams, trout, salmon, tuna


Meats – liver, beef, ham, chicken

Low-fat milk products


Swiss cheese

Low-fat yogurt


Nori/Seaweed


Fortified Foods


Nutritional Yeast

ABSORBABLE VITAMIN B12

METHYLCO-BALAMIN

ACTIVE FORM

FUNCTIONS (OR BENEFITS AS YOU AGE)

- Formation and maintenance of red blood cells (RBCs)
- Facilitates DNA synthesis
- Regulates homocysteine levels (decreases)
- Facilitates neurological functionting

DEFICIENCY & PATHWAY ALTERATIONS

- Increased production of homocysteine
- Decreased breakdown of homocysteine
- Circadian Rhythm Problems
- Cancers
- Memory-related disorders
- Cardiovascular diseases
- Fatigue
- Poor balance
- Mood disorders

VITAMIN D

FOOD SOURCES


Tuna


Mushrooms


Eggs


Mackerel


Cheese

Milk Products

BENEFITS AS YOU AGE


Lower Risk of Fractures


Improves Heart Function


Supports Immune System


Speeds Wound Healing

DEFICIENCY CAUSES

- Bone Pain
- Arthritis
- Obesity
- Backache
- Depression
- Diabetes
- Hypertension
- Osteoporosis
- Heart Disease
- Skin Conditions

MITOCHONDRIA

WAYS TO INCREASE MITOCHONDRIAL FUNCTIONING

Build muscle mass (strength conditioning)

Decrease toxin exposure (metals, persistent organic pollutants)

Vitamins
Glutathione
CoQ10
a-lipoic acid + acetyl-l-carnitine
Resveratrol
NAC
Vitamin E
PQQ
Ginkgo biloba
Proanthocyanidins

FUNCTIONS (OR BENEFITS AS YOU AGE)

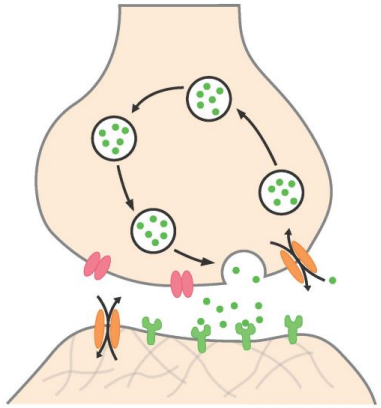
- Energy production for growth, movement & homeostasis
- Programmed cell death for dysfunctional, old cells
- Calcium signaling for neuron excitability, neurotransmission & plasticity (strengthening)

DEFICIENCY CAUSES

- Early Aging
- Neurological Disorders
- Diabetes
- Developmental Issues
- Psychiatric Disorders
- Cardiovascular Diseases
- Fatigue

NEUROTRANSMITTERS & PATHWAY

TRANSMIT INFORMATION FOR ESSENTIAL PROCESSES SUCH AS DIGESTION, BREATHING, HEARTBEAT, MOVEMENT, PAIN REGULATION ETC.



RELEVANT GENES

- **HTR2, TPH2, SLC6A4, MAO-A** genes are important in the synthesis, breakdown, transport and/or functioning of serotonin
- **COMT, MAO-A, MAO-B** genes are important for the breakdown of serotonin, norepinephrine and/or dopamine
- The **DBH** gene is important for norepinephrine synthesis
- The **GAD1** gene is important for GABA synthesis
- Variants in **COMT, MAO-A, MAO-B and GAD1** genes have been associated with mood, anxiety and focus issues

WAYS TO INCREASE LEVELS

Aerobic Exercise

Dietary Factors

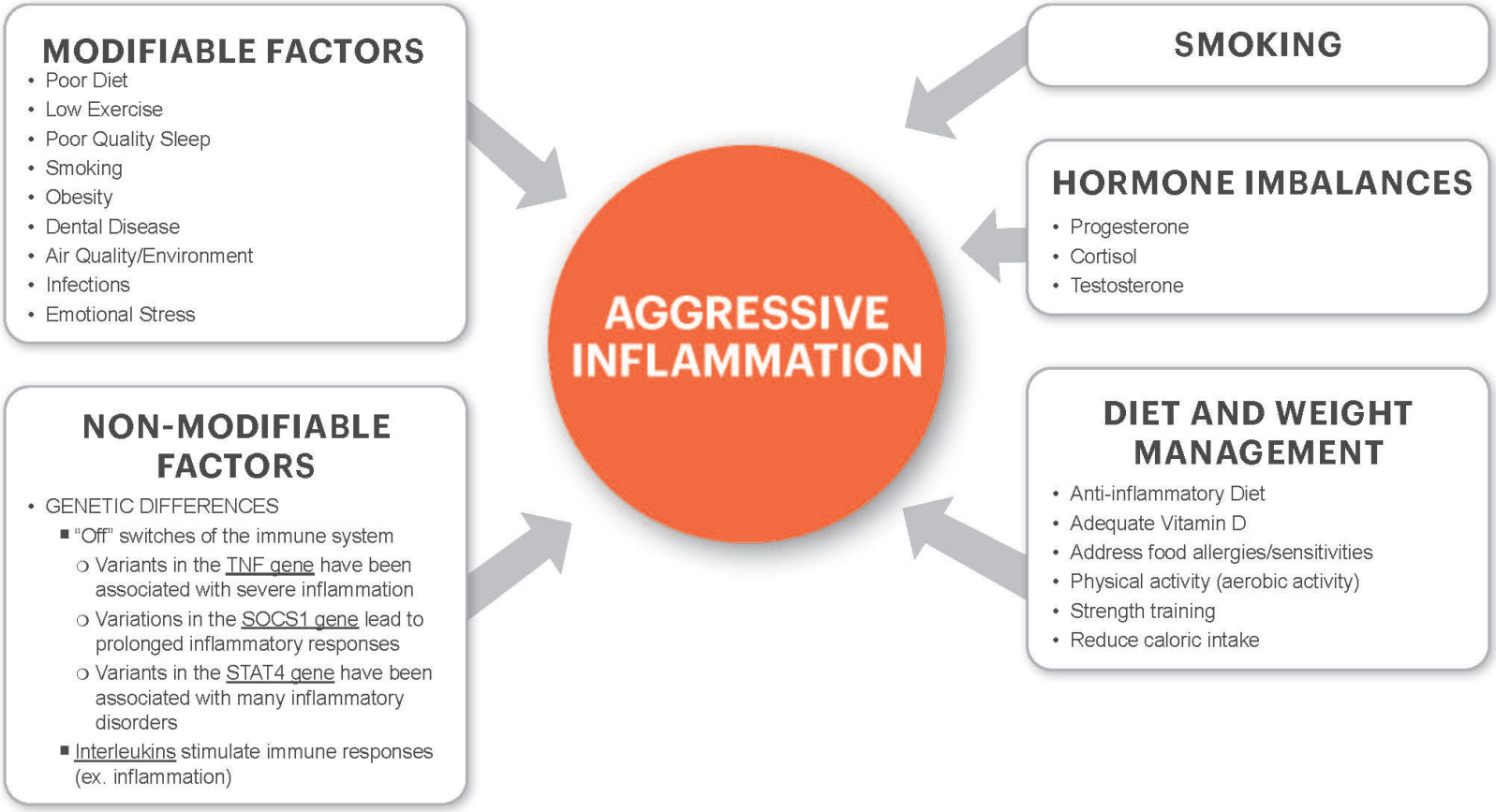
Mediation/Yoga

Increase Sun Exposure

ANTI-INFLAMMATORY

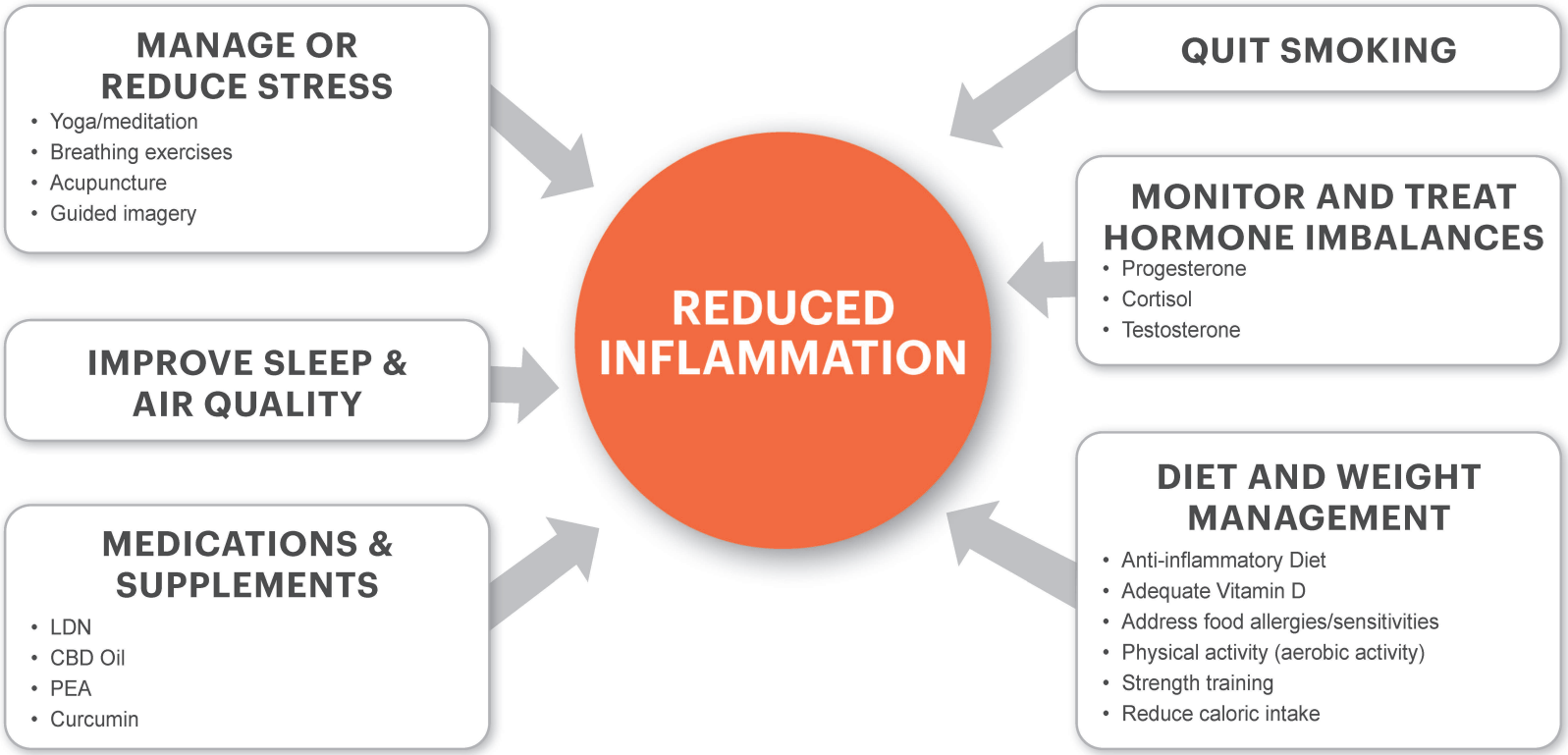
AN IMMUNE SYSTEM RESPONSE TRIGGERED BY HARMFUL STIMULI (EX. PATHOGENS, DAMAGED CELLS, TOXIC COMPOUNDS, IRRADIATION)

DRIVERS OF INFLAMMATION



ANTI-INFLAMMATORY

WAYS TO REDUCE INFLAMMATION

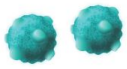


THE IMMUNE SYSTEM & AUTOIMMUNITY

WHAT DOES THE IMMUNE SYSTEM DO?

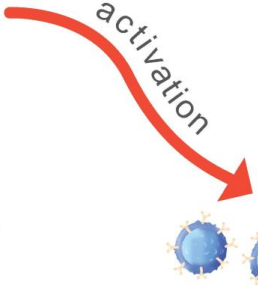
Prevent or limit infections by distinguishing between healthy and unhealthy cells

KEY PLAYERS & RELEVANT GENES



CYTOKINES
(ex. IL family, TNF-a)

- Helps with immune cell growth, activation, and function
- Interleukins (IL2, IL4, IL5, IL6, IL13, IL23R, IL2RA) stimulate the immune response
- SOCS1 & TNF are involved in cytokine signaling for the inflammatory response



LYMPHOCYTES
(ex. B, T & Natural Killer cells)

- Identify & kill infected cells
- Produces antibodies to fight future infections
- IDO1, CTLA4 & CD14 are involved in the suppression of T-cells
- C3, STAT4 & TRAF1 activate, form and/or differentiate T-cells

IMMUNE AGGRESSION

The immune system begins to attack healthy tissue

COMMON SYMPTOMS


Fatigue


Hair loss


Achy muscles


Inflammation


Skin rashes


Pain


Low-grade fever


Numbness and tingling in hands and feet


Trouble concentrating

MALFUNCTIONS LEAD TO

- Chronic inflammation
- Allergic reactions
- Immune aggressive diseases (Inflammatory bowel disease, skin & neurological disorders)

LOW-INFLAMMATORY

FOODS TO EAT

Fruits: strawberries, blueberries, cherries, oranges

Fatty fish: salmon, mackerel, tuna, sardines

Spices - turmeric, ginger

Green leafy vegetables & tomatoes

Dark chocolate

Olive oil

FOODS TO AVOID

Soda & other sugar-sweetened drinks

Dairy products

Fried foods

Red & Processed meats (hotdogs, sausage)

Refined carbohydrates: white bread, pastries

Margarine, shortening, lard

BENEFITS

Reduces inflammation

Reduces risk for cardiovascular disease & Type II diabetes

DETOXIFICATION

GLUTATHIONE IN DETOXIFICATION

Relevant genes for production are AHCY, CTH, GSTP1, GSTM1, GSTM3, GSR, MTRR & MTR

WHY IS IT IMPORTANT?

Maintains health by protecting the body from toxins

Regulates cell production and programmed cell death

Critical role in chemical detoxification

Vital for proper mitochondrial function

WAYS TO INCREASE GLUTATHIONE

- Limit alcohol intake
- N-acetyl-cysteine (NAC)
- Glutathione therapies
- (ie. IV Glutathione, Glutathione suppository, Lipsomal Glutathione)
- Include whey in diet, unless allergic or intolerant
- Methylation Support - if necessary

SUPEROXIDES & ANTIOXIDANTS

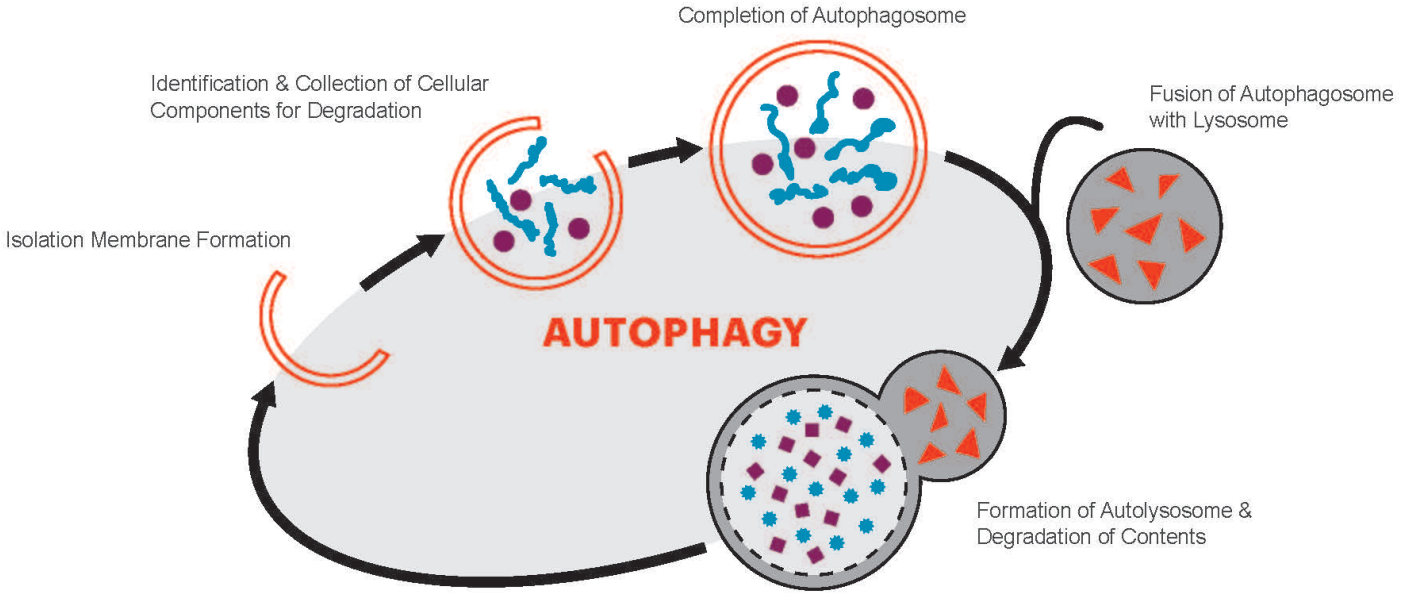
- SOD1, SOD2, SOD3 genes are important to transform superoxides to protect against mitochondrial damage
- Reactive Oxygen Species (ROS) can damage mitochondria and cause cell death.
- Antioxidants such as Vitamin A, Vitamin C and Vitamin E act as a defense against ROS

DEFICIENCY CAUSES

- Auto-immune diseases
- Cardiovascular diseases
- Neurodegenerative diseases
- Cell death
- Poor mitochondrial function

AUTOPHAGY

VARIANTS IN THE ATG GENES HAVE BEEN ASSOCIATED WITH CELLULAR BLOCKAGE



DEFECTS LEAD TO:

- Neurodegenerative Diseases
- Aging
- Heart Disease
- Developmental Disorders
- Type II Diabetes
- Insulin Resistance
- Fatty Liver
- Cancers

WAYS TO INCREASE

Intermittent fasting or low-calorie diet

Routine Exercise

Ketogenic diets (high fat, low carbs)

Medications & Supplements
D-Chiro Inositol (B8)
Metformin

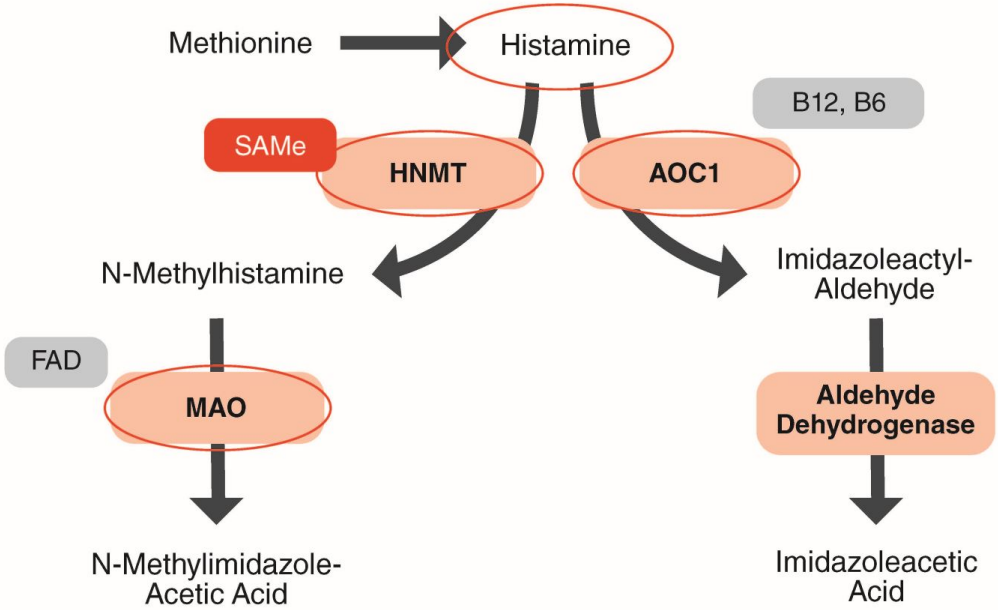
HISTAMINE

HISTAMINE

- Natural substance found in various foods

IMPLICATIONS

- Metabolic Enzymes: amine oxidases (ex. AOC1, MAO, DAO) & HNMT
- High histamine & low amine oxidase activity is associated with:
  - Diarrhea
  - Headaches
  - Nose congestion
  - Asthma
  - Hypotension
  - Arrhythmia
  - Flushing
  - Urticaria (hives)
  - Pruritus (itchy skin)
- Dietary histamine can be rapidly detoxified by amine oxidases, whereas persons with low amine oxidase activity are at risk of histamine toxicity



AOCI & HNMT POLYMORPHISM HISTAMINE

LOW HISTAMINE LEVEL FOODS

Meats & Fish
fresh meat (ex. chicken, turkey,pork and red meat),fresh fish (ex. hake, trout, plaice)

Egg yolk

Fresh fruits
(with the exception of strawberries)

Fresh vegetables

Grains

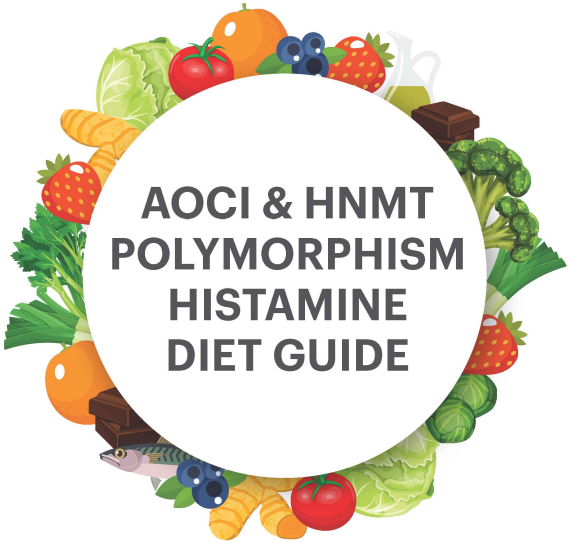
Milk substitutes
(Coconut milk, rice milk)

Cream cheese, butter

Most cooking oils

Most leafy herbs

Beverages
(non-citric fruit juices, herbal teas)



HIGH HISTAMINE LEVEL FOODS

Egg whites

Processed, cured, smoked and fermented meats/fish (lunch meat, bacon, sausage, pepperoni, canned tuna)

Leftover meat
(After meat is cooked, the histamine levels increase due to microbial action as the meat sits)

Dairy products: All fermented milk products (ex. aged cheeses, yogurt, buttermilk, kefir)

Beverages (Black Tea, alcohol)

Chocolate, cocoa

Fruits (oranges, grapefruit, lemons, lime, berries, dried fruit)

Vegetables (spinach, tomatoes, eggplant)

Artificial food colors and preservatives

Fermented & vinegar-containing foods
(sauerkraut, kombucha, pickles, relishes, ketchup, prepared mustard)

Spices (cinnamon, chili powder, cloves, nutmeg, curry powder, cayenne)

SELENIUM

WAYS TO INCREASE LEVELS

Brazil nuts

Low-fat milk products

Meats & seafood – fish (tuna, halibut, sardines), ham, shrimp, beef, liver, chicken, turkey

Boiled eggs

Wheat germ, Brewer's yeast

Whole grains (unless gluten free)

Supplements

FUNCTIONS

Role in proper thyroid function & thyroid hormone metabolism

Role in DNA synthesis

Role in reproduction

Protection from infection & oxidative damage

DEFICIENCY VS HIGH INTAKE

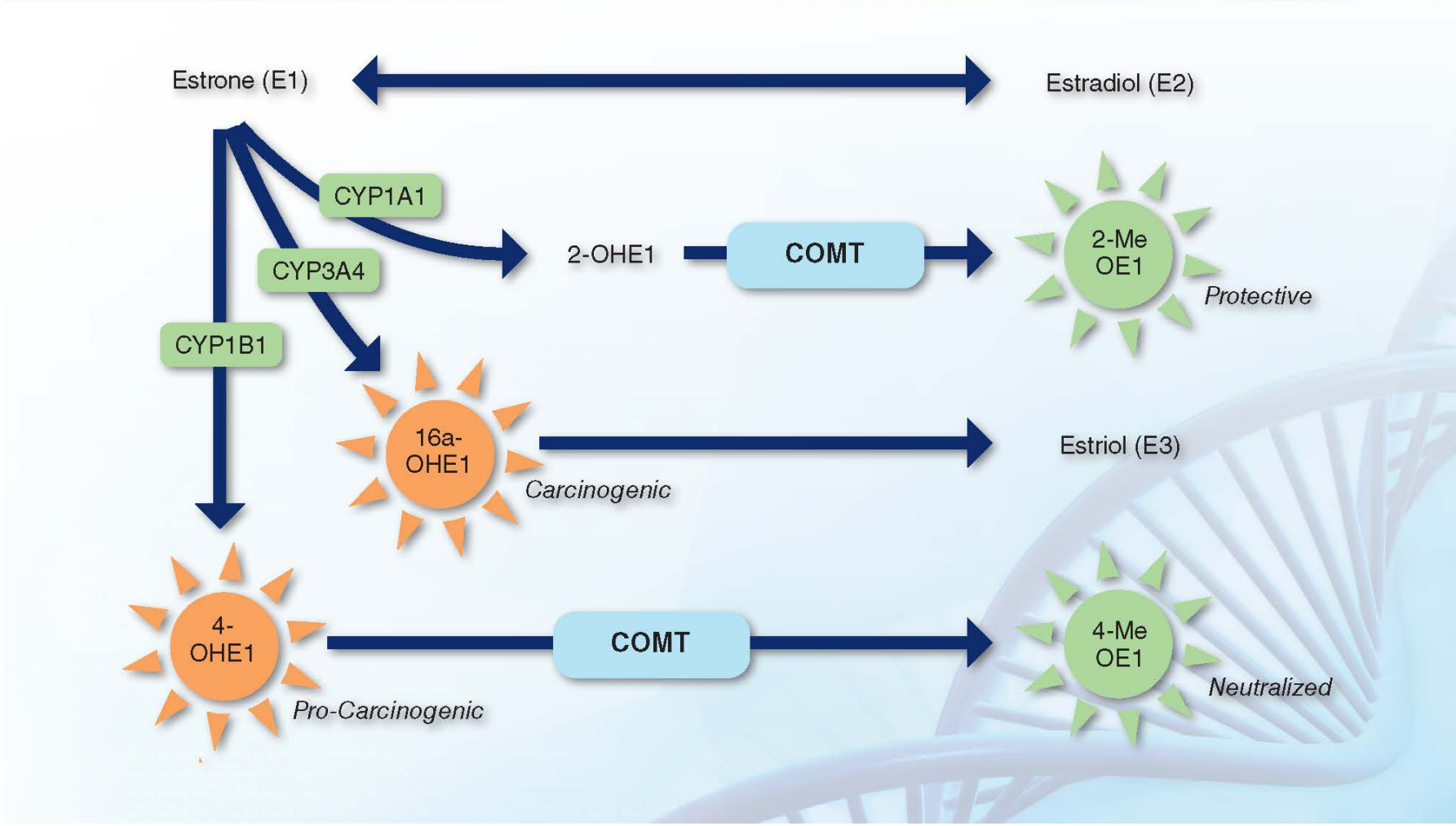
Deficiency

- Cardiovascular disorders
- Developmental issues
- Thyroid disorders
- Joint & bone issues
- Infertility issues
- Cancers

High intake

- Metallic taste in mouth
- Garlic odor of breath
- Hair and nail loss or brittleness
- Nervous system abnormalities
- Nausea
- Diarrhea
- Skin rashes
- Fatigue
- Irritability

Phase I and II - Estrogen Metabolism



HYPERTENSION RISK FACTOR

HIGH BLOOD PRESSURE

- Ranges
  - Normal: 120/80
  - Range of concern: 140/90 or higher
- Risk factors: high salt diet, high alcohol intake, stress, little potassium intake, alcohol & tobacco use, obesity, genetics/family history, age, lack of physical activity
- Uncontrolled high blood pressure has been associated with an increased risk for cardiovascular diseases and stroke

AGT & ACE GENES

Variants have been associated with an increased risk for:

Salt retention

Kidney issues

Preeclampsia

Poor sports performance

Hypertension & other cardiovascular issues

LIFESTYLE CHANGES

Limit salt intake

Angiotensin II Receptor Blockers (“sartans”)

Weight management & routine exercise

Mediterranean diet

Quit smoking

Heart-healthy diet/ Low-sodium diet/ DASH diet

DASH DIET

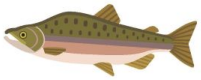
FOOD TO EAT

Fruits & vegetables

Egg whites

Whole grains (unless gluten free)

Nuts & nut butters



Lean, skinless meat & fish (salmon, trout, herring)

Legumes

Low-fat or fat-free dairy products

Olive oils high in polyphenols

BENEFITS

Improves heart health

Improves and/ or reduces risk for hypertension, heart disease and stroke

FOODS TO AVOID AND/OR LIMIT

Red meat

Fried foods

Sweets

Processed meats - deli meat, hotdogs, sausage, bacon

Sugar-sweetened beverages

Fats/oils - Butter, margarine, tropical oils (coconut, palm)

High-salt foods

Gene Information Key

rsID	Gene	"-" variant	"+" variant
rs4343	ACE	A	G
rs10156191	AOC1	C	T
rs26538	ATG12	T	C
rs10210302	ATG16L1	C	T
rs510432	ATG5	T	C
rs3733890	BHMT	G	A
rs2250656	C3	C	T
rs234706	CBS	A	G
rs2569190	CD14	G	A
rs4680	COMT	G	A
rs1021737	CTH	G	T
rs231775	CTLA4	A	G
rs1801222	CUBN	G	A
rs4646	CYP19A1	A	C
rs762551	CYP1A2	A	C
rs70991108	DHFR	DEL	INS
rs3211719	F10	A	G
rs6025	F5	C	T
rs2071010	FOLR1	G	A
rs492602	FUT2	A	G
rs3828275	GAD1	C	T
rs769407	GAD1	G	C
rs17883901	GCLC	G	A
rs8190955	GSR	G	A
rs1695	GSTP1	A	G
rs2187668	HLA-DQA1	C	T
rs7454108	HLA-DQB1	T	C
rs1800925	IL13	C	T
rs2069812	IL5	A	G

rsID	Gene	"-" variant	"+" variant
rs1800795	IL6	C	G
rs6323	MAOA	T	G
rs1799836	MAOB	C	T
rs1076991	MTHFD1	C	T
rs1801131	MTHFR: A1298C	T	G
rs1801133	MTHFR: C677T	G	A
rs1805087	MTR	G	A
rs1801394	MTRR	A	G
rs1801280	NAT2	T	C
rs6721961	NFE2L2	G	T
rs4795067	NOS2	A	G
rs1800566	NQO1	G	A
rs4704397	PDE8B	G	A
rs8192678	PPARGC1A	C	T
rs1467568	SIRT1	A	G
rs1051266	SLC19A1	T	C
rs33972313	SLC23A1	C	T
rs4880	SOD2	G	A
rs10181656	STAT4	C	G
rs526934	TCN1	A	G
rs1801198	TCN2	C	G
rs1937	TFAM	C	G
rs1800629	TNF	G	A
rs2274924	TRPM6	T	C
rs6994076	TTPA	A	T
rs2228570	VDR	G	A

Definitions

AUTOPHAGY	
ATG12	Autophagy-related 12 protein is part of the core autophagy machinery inside the cell. Autophagy, a form of cellular "recycling" is necessary for many cell functions. ATG12 is specifically involved in turning off the innate immune response. Mutations in the ATG12 gene are predicted to lead to increased activity of the innate immune response, and overall inflammation.
ATG16L1 rs10210302	The ATG16L1 (autophagy related 16 like 1) gene encodes a protein that is part of a major protein complex essential for autophagy, a process of digesting cellular components for nutrient sensing and cellular regulation. The polymorphism rs10210302 occurs in the promoter region of the gene, and a comprehensive study has linked the T allele with Crohn's disease, an inflammatory bowel disease.
ATG5	The ATG5 (autophagy-related 5) gene is an important intracellular mediator of the autophagy response, which is essential for maintaining homeostasis. The polymorphism rs510432 occurs in the promoter region of ATG5, and individuals homozygous for the C allele have been shown to have increased mRNA expression of ATG5. Additionally, individuals homozygous for the C allele are at an increased risk for developing childhood asthma, but they have a reduced risk for developing sepsis. Individuals who are heterozygous or homozygous for the T allele have been shown to have reduced levels of C-reactive protein.
DETOXIFICATION	Detoxification enzymes are responsible for clearing environmental chemicals and metabolites from our body. Accumulation of these chemicals and by-products can damage intracellular biochemical functions. Alterations in these systems can have a significant negative effect on the nervous system and immune systems functions. These polymorphisms can result in decreased "quality of life" and even decreased "life-span".
CTH	The CTH (cystathionine gamma-lyase) gene encodes an enzyme that catalyzes the last step in the transsulfuration of L-methionine to L-cysteine. More specifically, it converts cystathionine, derived from methionine, into cysteine, which is utilized in the liver to synthesis glutathione, a ubiquitous antioxidant. As a results, CTH has an important role in glutathione production. The polymorphism rs1021737 results in an isoleucine substitution for a serine residue in the enzyme at position 403. The T allele, which encodes the isoleucine variant, has been associated with an accumulation of homocysteine.
GCLC rs17883901	The GCLC (glutamate-cysteine ligase catalytic subunit) gene encodes the first and rate-limiting enzyme in glutathione biosynthesis. Glutathione is a potent, nonprotein antioxidant that has an important role in protecting cells from oxidative stress and xenobiotics. Therefore, a reduction in biosynthetic capacity through reduction of GCLC activity results in reduced antioxidant capacity and activity of enzyme that use glutathione as a cofactor, such as glutathione transferase and glutathione peroxidase. The polymorphism rs17883901 occurs in the promoter region of the gene, and mechanistic studies have found that the variant encoded by the A allele reduces promoter activity by as much as 60% in cell models. Furthermore, A allele carriers had significantly increased risk for coronary heart disease and heart attack. Lastly, plasma glutathione levels were reduced in individuals with the AA genotype.
GSR rs8190955	The GSR (glutathione-disulfide reductase) gene encodes a riboflavin-dependent enzyme that reduces oxidized glutathione (GSSH) to its antioxidant form (GSH). Therefore, GSR is essential for maintaining adequate glutathione levels and cellular antioxidant capacity. The polymorphism rs8190955 results in a cysteine substitution for an arginine residue at position 153. Mechanistic studies have shown that the A allele, which encodes a cysteine residue, produces an enzyme that is less stable than the version produced by the G allele. Furthermore, the instability was predicted to reduce enzyme function, and the A allele has been associated with obstructive heart defects and hereditary anemia.
GSTP1	The GSTP1 (glutathione S?transferase pi 1) gene encodes a cytosolic enzyme that has a keystone role in cellular detoxification. It conjugates cytotoxic and carcinogenic substances to glutathione for elimination, thereby aiding in antioxidant defense and preserving DNA integrity. The polymorphism rs1695 results in a valine substitution for an isoleucine residue in the enzyme at position 105, which is a region of the protein that is known to undergo several post-translational modifications. Mechanistic studies have shown that the protein produced by the G allele, which encodes a valine residue, has reduced substrate binding capacity and enzymatic activity. Numerous clinical studies have shown that the GG genotype is a risk factor for asthma, especially when individuals are exposed to environmental toxins, such as cigarette smoke or traffic-related air pollution. Additionally, the G allele is associated with increased risk for heart failure, and the frequency of the G allele is decreased in populations of older, living adults, suggesting it does not confer increased longevity.
NAT2 rs1801280	The NAT2 (N-acetyltransferase 2) gene encodes an enzymes that catalyzes the transfer of an acetyl group from acetyl coenzyme A to compounds with aromatic amines, hetrocyclic amines, or hydrazine structures. Therefore, NAT2 has an important role in the metabolism and elimination of a large number of pharmaceutical drugs and environmental toxins. The polymorphism rs1801280 results in a threonine substitution for an isoleucine residue at position 114. The C allele, which encode a threonine residue, defines the NAT2*5B haplotype, which has been found to have slow acetylation activity. Consistent with this status, carriers of the C allele are at increased risk for various types of cancer and adverse drug reactions. Additionally, increased toxin exposure, such as frequent or intense smoking, can further increase these risks.
NFE2L2 rs6721961	The NFE2L2 (NFE2 like bZIP transcription factor 2) gene encodes a transcription factor, known as NRF2, that has a crucial role in the regulation of a network of antioxidant genes. NRF2 activates expression of genes with a conserved promoter sequence called the antioxidant response elements (ARE). Genes with an ARE include superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX), etc. Therefore, NRF2 is a master regulator of oxidant and antioxidant balance. The polymorphism rs6721961 occurs in the promoter region of NFE2L2, and mechanistic studies have found that the variant encoded by the T allele has reduced promoter activity and mRNA levels. Consistent with these findings, carriers of the T allele have been shown to have lower total antioxidant capacity. T allele carriers had less SOD, CAT, GPX, and glutathione activity. Furthermore, T allele carriers are at increased risk for insulin resistance and vascular stiffness.

SOD2	The SOD2 (superoxide dismutase 2) gene encodes a mitochondrial matrix enzyme that uses iron and manganese to covert superoxide, a byproduct of the electron transport chain, to hydrogen peroxide and oxygen. Moreover, SOD2 participates in phase 1 detoxification to initiate the transformation of highly reactive oxygen species to a less reactive intermediary metabolite. Hydrogen peroxide, the intermediary metabolite produced by SOD2 activity, requires further detoxification by phase 2 enzymes, such as catalase or glutathione peroxidase. Nevertheless, SOD2 function is crucial to initiate the detoxification process of reactive oxygen species in the mitochondria, aiding in protection against oxidative damage. The polymorphism rs4880 results in a valine substitution for an alanine residue in the enzyme at amino acid position 16, which occurs in the mitochondrial targeting sequence. Mechanistic studies have shown that the A allele, which encodes a valine residue, has incomplete transfer to the mitochondria due to a conformational change in the targeting sequence. Furthermore, studies in animal models have shown that the enzyme encoded by the A allele has decreased formation of active enzyme in the mitochondrial matrix, and clinical studies have found individuals with the AA genotype to have less SOD2 activity. Consistently, individuals with the AA genotype have been shown to have decreased plasma total antioxidant status and increased markers of oxidative stress and lipid peroxidation. However, implementation of a healthy diet and exercise intervention has been shown to reduce markers of lipid peroxidation in those with the AA genotype. Lastly, the AA genotype was associated with increased risk for coronary heart disease.
ESSENTIAL MINERALS	The polymorphisms in this panel will identify any potential weakness of absorption or delivery or your essential minerals..
TRPM6	The TRPM6 (transient receptor potential cation channel subfamily M member 6) gene encodes a membrane transporter that is essential for magnesium homeostasis. TRPM6 is expressed in gut and kidneys, and it is needed for magnesium absorption. The polymorphism rs2274924 results in a nucleotide change that causes translation of the transporter to terminate prematurely, resulting in a truncated version of the transporter that is approximately 500 amino acids shorter than the full-length protein. Carriers of the C allele, which encodes the truncated protein, are at increased risk for hypomagnesemia, with individuals with the CC genotype at greater risk.
ESSENTIAL VITAMINS	The polymorphisms in this panel will identify any potential weakness of absorption, conversion or delivery or your essential vitamins.
SLC23A1	The SLC23A1 (solute carrier family 23 member 1) gene encodes a sodium-dependent vitamin C transporter required for the absorption of vitamin C and its distribution to tissues throughout the body. The polymorphism rs33972313 results in a leucine substitution for a valine residue at amino acid position 264, which occurs in a transmembrane domain of the transporter. The T allele, which encodes a leucine residue, has been associated with decreased levels of vitamin C, and levels were further reduced in individuals with the TT genotype.
TTPA rs6994076	The TTPA (alpha tocopherol transfer protein) gene encodes a carrier protein that binds alpha-tocopherol, the predominate form of vitamin E in the body, and facilities its export from the liver to circulation. The polymorphism rs6994076 occurs in the promoter region of the gene, and mechanistic studies found that the variant encoded by the T allele reduces transcription of TTPA. In clinical studies, carrier of the T allele had lower levels of circulating vitamin E.
VDR rs2228570	The VDR (vitamin D receptor) gene encodes a receptor for vitamin D3 that is highly expressed in the intestines. VDR is a member of the nuclear hormone receptor superfamily, so when activated by vitamin D, it can impact transcription of many genes involved in mineral metabolism, cell proliferation, and immune activation. The polymorphism rs2228570, sometimes termed FokI for the restriction enzyme that can detect it, results in a threonine substitution for a methionine residue in the first codon of the protein, altering the translation start site. As a result, translation of the receptor produced by the A allele, which does not contain the FokI restriction site (f) and encodes a methionine residue, is 427 amino acids in length, whereas the receptor produced by the G allele, which does contain the FokI restriction site (F) and encodes a threonine residue, is three amino acids shorter. Mechanistic studies indicate that the shorter variant encoded by the G allele has greater capacity to bind vitamin D and more transcriptional activity in response to vitamin D. Consistent with these findings, A allele carriers were less responsive to vitamin D supplementation, and A allele carriers were shown to have reduced calcium absorption and bone mineral density. Furthermore, vitamin D supplementation was less effective at reducing inflammatory markers in carriers of the A allele, and the A allele is associated with risk for celiac disease and type 2 diabetes.
ESTROGEN METABOLISM AND CLEARANCE	The conversion of estrogen and its' metabolites is essential to effective safe estrogen treatment. These SNPs will identify your potential for increased production of possible carcinogenic forms of estrogen
CYP19A1	The CYP19A1 (cytochrome P450 family 19 subfamily A member 1) gene encodes a monooxygenase enzyme termed aromatase. Aromatase catalyzes the last step in the conversion of androgens to estrogen. The polymorphism rs4646 occurs in the 3' untranslated region, suggesting that it might affect gene expression by altering mRNA stability. Furthermore, the C allele has been associated with higher circulating estrogen levels, indicating increased aromatase activity.
GASTROINTESTINAL	
AOC1	The AOC1 (amine oxidase copper-containing 1) gene encodes for the diamine oxidase (DAO) enzyme, which is one of two enzymes that breaks down pro-inflammatory amines such as histamine and putrescine. DAO is active in intestinal mucosal cells, and a deficiency of its activity results in the accumulation of high levels of histamine, which can cause a wide range of neurological, gastrointestinal, and epidermal disorders. The polymorphism rs10156191 results in a methionine substitution for a threonine residue in the enzyme at position 16. The T allele, which encodes the methionine variant, results in an enzyme with lower metabolic capacity than the enzyme encoded by the C allele, possibly resulting in reduced ability to break down histamine.
FUT2	The FUT2 (fucosyltransferase 2) gene encodes an enzyme involved in the synthesis of histoblood group antigens (HBGA), which are found on the intestinal mucosa and various bodily fluids. HBGA are oligosaccharide molecules, and in the intestinal mucosa, they act as an attachment site and nutrient source for intestinal bacteria. The polymorphism rs492602 is in near perfect linkage disequilibrium with rs601338, meaning that the alleles are nonrandomly associated and inherited together. Therefore, the G allele for rs492602 indicates the inheritance of the minor allele for rs601338, which results in a stop gain mutation that produces a truncated version of FUT2 that is unable to secrete the oligosaccharide molecules. As a result, individuals of the GG genotype for rs492602 are considered "non-secretors". Carriers of the G allele were found to have compositional and functional changes to the gut microbiota and reduced microbial diversity. Furthermore, G allele carriers had increased susceptibility for inflammatory bowel disease.

HLA-DQA1	The HLA-DQA1 (major histocompatibility complex, class II, DQ alpha 1) gene encodes a cell surface protein that plays a central role in the function of the immune system and the development of autoimmune disease. HLA-DQA1 is a class II, human leukocyte antigens (HLA), which are expressed on the surface of antigen presenting cells where HLA can bind antigens or substances that induce an immune response for recognition by T cells. HLA-DQA1 encodes a component of HLA-DQ2, a serotype or distinct variation among the HLA structure that determines its antigenic complements. More specifically, the T allele for the polymorphism, rs2187668, can be used to identify HLA-DQ2.5, a high-risk factor for gluten sensitivity and celiac disease. Consistently, genome-wide association studies have found the T allele is associated with celiac disease.
HLA-DQB1 rs7454108	The HLA-DQB1 (major histocompatibility complex, class II, DQ beta 1) gene encodes a cell surface protein that plays a central role in the function of the immune system and the development of autoimmune disease. HLA-DQB1 is a class II, human leukocyte antigens (HLA), which are expressed on the surface of antigen presenting cells where HLA can bind antigens or substances that induce an immune response for recognition by T cells. More specifically. The C allele for the polymorphism, rs7454108, can be used to identify HLA-DQ8, a serotype or distinct variation among the HLA structure that determines its antigenic complements. HLA-DQ8, for example, is a high-risk factor for gluten sensitivity and celiac disease.
HEALTH PRECAUTIONS	
ACE	The ACE (angiotensin-converting enzyme) gene encodes a protein that plays a crucial role in regulating blood pressure and maintaining electrolyte balance. It converts angiotensin I to the active form, angiotensin II, which leads to vasoconstriction and elevated blood pressure. The polymorphism rs4343 confers an insertion/deletion of a small DNA sequence in the gene. Carriers of the G allele display increased ACE activity and elevated plasma levels of angiotensin II. Additionally, carriers of the G allele are more prone to blood pressure spikes when consuming high-salt diets than individuals with the AA genotype. Heterozygous individuals display an intermediate phenotype.
CYP1A2	The CYP1A2 (cytochrome P450 family 1 subfamily A member 2) gene encodes a monooxygenase enzyme that mainly functions in the liver. It catalyzes the metabolism of about 10% of clinically used drugs that are metabolized by CYP enzymes, including caffeine. Additionally, it metabolizes some endogenous compounds, such as melatonin and estradiol. The A allele of rs762551 was found to have higher CYP1A2 enzyme activity with exposure to smoking or heavy coffee consumption. In contrast, the C allele was found to be associated with lower enzyme activity. rs762551 was also associated with caffeine consumption. Specifically, the AA genotype may predispose an individual to have higher coffee intake.
Factor V	The F5 gene encodes for coagulation factor V, an essential component of the blood coagulation cascade. Specifically, it serves as a cofactor for the prothrombinase activity of factor Xa that results in the activation of prothrombin to thrombin. The polymorphism rs6025 is a well-known missense mutation known as the Leiden mutation. The T allele of rs6025 encodes for a variant in which glutamine is substituted for arginine at position 506. Carriers of the T allele are at an elevated risk for venous thromboembolism and related conditions with the risk being even higher in individuals homozygous for the T allele.
Factor X	The F10 (coagulation factor X) gene encodes a vitamin K-dependent factor in the blood coagulation cascade. Factor X (FX) plays an important role in blood clotting, as both the intrinsic and extrinsic coagulation pathways converge on FX activation. FX is translated as a preproprotein, which is processed to a mature and activated version that converts prothrombin to thrombin. The polymorphism rs3211719 occurs in intron 1, and genome-wide association studies have found that the G-allele is associated with decreased prothrombin time and increased levels of factor VII, which initiates the extrinsic coagulation pathway. Additional studies have shown that the G allele is associated with increased factor VII antigen and factor VII coagulant activity, suggesting that clotting propensity is increased.
HOMOCYSTEINE METABOLISM	
BHMT rs3733890	The BHMT (betaine-homocysteine S-methyltransferase) gene encodes an essential enzyme that consume betaine, or trimethylglycine, to convert homocysteine to dimethylglycine and methionine. Therefore, BHMT both detoxifies homocysteine and generates methionine needed to maintain methylation capacity. It is primarily expressed in the liver and kidneys. The polymorphism rs3733890 results in a glutamine substitution for an arginine residue at position 239. The A allele, which encodes a glutamine residue, results in more partitioning of choline, a precursor of betaine, for phosphatidylcholine synthesis via the cytidine diphosphate (CDP)-choline pathway, suggesting that less betaine is available for detoxification of homocysteine and regeneration of methionine. Likewise, carriers of the A allele have been shown to have reduced levels of betaine and dimethylglycine. Furthermore, folate was shown to be a less effective treatment to lower homocysteine levels in carrier of the A allele with hyperhomocysteinemia. Nevertheless, increased intake of choline in A allele carriers can increase flux to betaine synthesis to support BHMT activity. In summary, A allele carriers may benefit from increased choline or betaine intake, especially when managing high levels of homocysteine.
CBS rs234706	The CBS (cystathionine beta-synthase) gene encodes an enzyme that catalyzes the first step in the transsulfuration pathway. More specifically, CBS, a pyridoxal 5'-phosphate-dependent enzyme, consumes serine to convert homocysteine to cystathionine, which is further catabolized to generate substrate for glutathione synthesis. Therefore, homocysteine clearance and glutathione synthesis converge on the function of CBS. The polymorphism rs234706 results in a nucleotide substitution in exon 8. Carriers of the G allele have been found to have higher levels of homocysteine and lower levels of cystathionine and betaine, consistent with reduced CBS activity. Furthermore, individuals with the GG genotype had higher plasma homocysteine following the ingestion of a methionine load, and individuals with the GG genotype were less responsive to folate supplementation to lower homocysteine levels. Lastly, the GG genotype is associated with increased risk for coronary artery disease.

MTR	The MTR (5-methyltetrahydrofolate-homocysteine methyltransferase) gene encodes a metabolic enzyme that catalyzes the remethylation of homocysteine to methionine; therefore, the enzyme is also referred to as methionine synthase. The reaction requires both active vitamin B9 (methyltetrahydrofolate) and vitamin B12 (methylcobalamin), and the enzyme works in close coordination with 5-methyltetrahydrofolate-homocysteine methyltransferase reductase (MTRR), which regenerates MTR to a functional state. The polymorphism rs1805087 results in a glycine substitution for an aspartic acid residue in the enzyme at position 919, which is located in the binding site for accessory proteins needed to regenerate the enzyme to its active form. Numerous studies indicate that the G allele variant, which encodes a glycine residue, results in increased enzyme function. For example, the G allele was associated with reduced levels of homocysteine and increased levels of DNA methylation, suggesting accelerated conversion of homocysteine to methionine. However, increased MTR activity also results in accelerated consumption of methylcobalamin, and predictably, the GG genotype has been associated with vitamin B12 deficiency. Nevertheless, A allele carriers may have decreased methionine synthesis, which is essential for production of S-adenosyl methionine (SAMe) and maintenance of methylation capacity.
INFLAMMATORY	This Enzyme category has significant effects on the inflammatory state of a person's body. Polymorphisms in these specific enzymes will significantly increase the levels of inflammation in the body. By supplementing these enzyme deficiencies, the patient will effectively reduce inflammatory damage to the body.
C3 rs2250656	The C3 (complement C3) gene encodes an abundant protein in the complement cascade, a major component of the innate immune system. C3 is secreted into the bloodstream, and activation of C3 is essential for both classical and alternative complement activation. The polymorphism rs2250656 occurs in the fourth intron, and carriers of the T allele were shown to have increased plasma levels of C3 and C-reactive protein, two markers of inflammation. Additionally, increasing consumption of n-6 PUFAs, which are known to have a proinflammatory effect, further increased plasma levels of C3 in individuals with the TT genotype. Lastly, T allele carriers had a 2-fold higher risk for metabolic syndrome compared to individuals with the CC genotype, and the T allele was associated with severe COVID-19, suggesting that the T allele confers increased complement activity and inflammation.
CD14 rs2569190	The CD14 (CD14 molecule) gene encodes a crucial determinate of the innate immune response and protector from atopy. CD14 is an endotoxin receptor that is expressed on the surface of monocytes and macrophages. The polymorphism rs2569190 occurs in the promoter region of the gene, and mechanistic studies have shown that the variant encoded by the A allele is preferentially bound by RNA polymerase, suggesting that there is increased transcription of the A allele variant. Consistent with this mechanism, carriers of the A have been shown to have increased levels of CD14. Clinical studies have found that while A allele carriers have basal IgE levels that are lower than G allele carriers, IgE levels rise to a greater extent in A allele carriers when exposed to various forms of endotoxins. Moreover, A allele carriers are at increased risk for asthma or allergic disease when highly exposed to endotoxins, suggesting that A allele carriers are at increased risk for environmentally instigated inflammation. Lastly, A allele carriers may have increased risk for cardiovascular disease and inflammatory bowel disease, both of which are characterized by increased inflammation.
CTLA4	The CTLA4 (cytotoxic T-lymphocyte associated protein 4) gene encodes a cell-surface receptor that acts as an important inhibitor of T cell activity and T cell-mediated immune responses. Therefore, CTLA4 has a crucial role in T cell homeostasis and self-tolerance, the loss of which can lead to the development of autoimmunity. The polymorphism rs231775 results in an alanine substitution for a threonine residue in the receptor at position 17, and the G allele, which encodes the alanine variant, results in decreased expression and cell surface localization of CTLA4 and increased proliferative response of T cells. Furthermore, clinical studies found that the G allele was associated with a variety of autoimmune diseases, such as autoimmune thyroid disease, type 1 diabetes, and rheumatoid arthritis. Additionally, the GG genotype was associated with positivity for insulinoma associated-2 autoantibodies (IA-2A) in patients with type 1 diabetes.
IL13	The IL13 (interleukin 13) gene encodes a cell signaling molecule that has a central role in the regulation of allergic inflammation. IL13 has a crucial role in the activation of Th2 immune responses, including the stimulation of B cells to synthesize IgE, a type of immunoglobulin that mediates allergic reactions. The polymorphism rs1800925 is located in the promoter region the gene, and functional studies have shown that the variant encoded by the T allele increases transcription of IL13 by increasing the binding of STAT transcription factors to the promoter region. Consistent with these studies, the TT genotype was found to be more prevalent in individuals with asthma and atopic dermatitis, and it has been associated with increased risk of sensitization to food and outdoor allergens. Additionally, the TT genotype was associated with increased risk for appendicitis, and the T allele was associated with increased risk for chronic obstructive pulmonary disease (COPD).
IL5	The IL5 (interleukin 5) gene encodes a cytokine that promotes the growth, differentiation, and activation of eosinophils. Therefore, it has an important role in Th2 immune responses and the development of allergic disease, which includes the promotion of IgE production and eosinophil response. The polymorphism rs2069812 is associated with a Th2-dominant autoimmune thyroid disease known as Graves' disease (GD). Carriers of the G allele have been shown to be at increased risk for GD as well as Graves' ophthalmopathy. Additionally, genome-wide association studies have linked the G allele with asthma, whereas the A allele has been associated with remission of GD and reduced risk of asthma.
IL6	The IL6 (interleukin 6) gene encodes a cytokine with pro- and anti-inflammatory functions depending on the context; however, continuous and dysregulated synthesis of IL6 plays a key role in both acute and chronic inflammation. Additionally, IL6 is a crucial link between the innate and adaptive immune systems, and the gene is known to be mainly regulated at the transcriptional level. The polymorphism rs1800795 occurs in the promoter region of the gene, and mechanistic studies showed that the C allele yielded lower levels of IL6 than the G allele. As a result, the G allele has the potential to increase the potency of any immunological response stimulated by IL6, and the G allele has been associated with conditions of high inflammation. For example, the G allele may increase the risk for rheumatoid arthritis, IBS, and various types of liver disease. Additionally, the GG genotype may increase the risk for psoriasis, poly cystic ovarian syndrome, and pre-term birth, all conditions associated with high levels of circulating IL6.

NOS2	The NOS2 (nitric oxide synthase 2) gene encodes an isoform of an enzyme that can be induced by pro-inflammatory agents like lipopolysaccharide and cytokines to produce nitric oxide (NO), a potent signaling molecule that can influence immune activation, inflammation, and cell survival. NOS2 can be conditionally activated in many cell types, but it is especially important for the function of immune cells, like macrophages. While NO is needed to defend against invading pathogens and unregulated cellular proliferation, excessive NO can damage healthy tissue. Carriers of the G allele for rs4795067 have an increased ratio of nitrite to nitrate in plasma. Because NO is quickly metabolized to nitrite in the body, nitrite is considered to be a measure of NO reserve, suggesting that carriers of the G allele have increased production of NO. Additionally, the G allele is associated with psoriasis, and NOS2 expression has been shown to be increased in psoriatic lesions. In summary, studies suggest that G allele carriers for rs4795067 produce increased amounts of NO, which can lead to inflammation.
STAT4	The STAT4 (signal transducer and activator of transcription 4) gene encodes a transcription factor that responds to extracellular growth factors and cytokines. It is present in the cytosol, and following cytokine signaling at the cell surface, STAT4 is phosphorylated and translocates to the nucleus, initiating the expression of cytokines, receptors, and signaling factors. The polymorphism rs10181656 occurs in the third intron, and cell-based experiments indicate that the G allele results in overexpression of STAT4, suggesting that the variant regulates gene expression. The G allele has also been associated with increased risk for numerous autoimmune diseases, such as rheumatoid arthritis, type 1 diabetes, lupus, and autoimmune thyroid disease. Furthermore, multiple studies support that there is additional disease risk for individuals carrying two copies of the G allele (GG genotype) compared to single allele carriers (GC genotype).
TNF-?	The TNF-? (tumor necrosis factor alpha) gene encodes an important pro-inflammatory cytokine that is mainly secreted by activated macrophages and monocytes. TNF-? functions in a plethora of biological functions from pathogen defense to tissue remodeling as it plays a role in cell survival, growth, and differentiation. Given its pro-inflammatory nature, dysregulation of TNF-? is also associated with numerous pathological conditions. The polymorphism rs1800629 occurs in the promoter region of the gene, and mechanistic studies have shown that the variant encoded by the A allele results in increased transcription and secretion of TNF-?. Therefore, the A allele has the potential to increase the potency of any immunological response stimulated by TNF-?. Consistent with this mechanism, the A allele has been associated with increased susceptibility to autoimmune disease, such as asthma, Graves' disease, psoriatic arthritis, and lupus. Additionally, individuals with the AA genotype were less responsive to TNF-? blockers for the treatment of autoimmune disease, and A allele carriers experienced fewer anti-inflammatory benefits of physical activity compared to individuals with the GG genotype. Similarly, obese individuals with the AA genotype were less responsive to a hypocaloric diet high in polyunsaturated fats as an intervention to improve metabolic markers. In summary, these results suggest that the inflammation generated by increased transcription of TNF-? caused by the A allele variant is markedly resistant to repression.
METABOLIC RISK FACTOR	The polymorphisms in this category relate to increase risk of developing metabolic syndromes including diabetes, fatty liver, hypothyroidism and insulin resistance.
PDE8B rs4704397	The PDE8B (phosphodiesterase 8B) gene encodes a enzyme that catalyzes the hydrolysis of cAMP, a second messenger crucial for cellular energy sensing. The polymorphism rs4704397 occurs in the first intron, and numerous studies have found that the A allele is associated with increased levels of TSH, consistent with hypothyroidism. Additionally, the A allele has been associated with sub-clinical hypothyroidism, hypothyroidism, and infertility.
METHYLATION	Methylation is a primary biochemical process in the body that involves the addition of a "methyl" chemical group to a vitamin or neurotransmitter. The addition of the "methyl" group allows for very specific biochemical interactions. Poor "methylation" function alters the effectiveness, delivery and function of many vitamins and important chemicals in the cell.
CUBN rs1801222	The CUBN (cubilin) gene encodes a receptor for intrinsic factor-cobalamin (Cbl-IF) complexes, and it is essential for intestinal absorption of vitamin B12. The polymorphism rs1801222 results in a phenylalanine substitution for a cysteine residue at position 253 in the protein. The A allele, which encodes a phenylalanine residue, is associated with reduced plasma levels of vitamin B12 and increased levels of homocysteine. Additionally, the A allele has been associated with risk for neural tube defects.
DHFR rs70991108	The DHFR (dihydrofolate reductase) gene encodes an enzyme essential for converting folic acid, a synthetic form of folate that is common in supplements and fortified foods, to tetrahydrofolate, a usable form of folate. The polymorphism rs70991108 results in a 19-bp deletion in the first intron, and mechanistic studies indicate that the deletion reduces translation and stability of the enzyme. Individuals homozygous for the deletion had higher levels of circulating unmetabolized folic acid, compared to carriers of the full length gene. Furthermore, cognitive function was reduced in deletion carriers, suggesting the 19-bp deletion reduces DHFR activity and folate metabolism. Lastly, the deletion allele has been associated with neural tube defects, pre-term delivery, and hepatic toxicity in response to treatment with methotrexate, which competitively inhibits DHFR activity. In summary, individuals with the 19-bp deletion should prioritize natural forms of folate, instead of folic acid, to maintain productive folate metabolism.
FOLR1	The FOLR1 (folate receptor alpha) gene produces a folate receptor that is responsible for transporting folate and its derivatives into cells. Variations in this gene can affect the delivery of folate in the bloodstream to cells. A study found that individuals who were heterozygous for the polymorphism rs2071010 had elevated serum folate levels compared to those with the GG genotype, suggesting that the A allele may reduce FOLR1 function. Additionally, individuals with the AA genotype may be at increased risk for elevated homocysteine levels.
MTHFD1	The MTHFD1 (methylenetetrahydrofolate dehydrogenase, cyclohydrolase, and formyltetrahydrofolate synthetase 1) gene encodes an enzyme that is essential for folate metabolism. The enzyme catalyzes three sequential steps in folate metabolism, utilizing separate catalytic domains in the protein. It converts 1) tetrahydrofolate (THF) to 10-formylTHF 2) 10-formylTHF to 5,10-methenlyTHF, and 3) 5,10-methenlyTHF to 5,10-methyleneTHF, which can then be converted to the bioactive form of folate, 5-methylTHF (MTHF), by methylenetetrahydrofolate reductase (MTHFR). The polymorphism rs1076991 occurs in the promoter region of the gene, and mechanistic studies found that the variant encoded by the T allele had a 60% reduction in transcription rate, suggesting that T allele carriers produce significantly less enzyme and MTHF. Congruently, the T allele has also been associated with risk for heart attack.

MTHFR rs1801131	The MTHFR (methylenetetrahydrofolate reductase) gene encodes a metabolic enzyme that catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (MTHF), the bioactive form of folate. Folate is a crucial mediator of one-carbon metabolism, which is necessary for a plethora of biochemical functions, such as nucleotide biosynthesis, amino acid metabolism, epigenetic maintenance, and oxidative defense. The polymorphism rs1801131, sometimes referred to as A1298C, results in an alanine substitution for a glutamate residue in the enzyme at position 429, which occurs near the binding site for an allosteric inhibitor, S-adenosyl-L-methionine (SAMe). Cell-based assays have shown that the enzyme produced by the G allele, which encodes an alanine residue, reduces MTHFR activity by about 30% compared to the enzyme produced by the T allele. Consistent with these findings, the GG genotype has been associated with increased risk for ischemic stroke and infertility due to decreased sperm production in men. Furthermore, individuals heterozygous for rs1801131 and rs1801133, another polymorphism in the MTHFR gene, have a more severe clinical phenotype that is similar to the AA genotype for rs1801133. Lastly, despite the prevalence of both minor alleles, the genotype combination rs1801131 GG and rs1801133 AA is nearly nonexistent in the population, suggesting it confers a significant genetic disadvantage.
MTHFR rs1801133	The MTHFR (methylenetetrahydrofolate reductase) gene encodes a metabolic enzyme that catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (MTHF), the bioactive form of folate. Folate is a crucial mediator of one-carbon metabolism, which is necessary for a plethora of biochemical functions, such as nucleotide biosynthesis, amino acid metabolism, epigenetic maintenance, and oxidative defense. The polymorphism rs1801133, sometimes referred to as C677T, results in a valine substitution for an alanine residue in the enzyme at position 222, which occurs near the binding site for a cofactor and the substrate, FAD and 5,10-methylenetetrahydrofolate respectively. Mechanistic studies have shown that the enzyme produced by the A allele, which encodes a valine residue, has reduced thermal stability and 55% reduced activity compared to the enzyme produced by the G allele. Consistent with these results, carriers of the A allele were found to have decreased levels of folate and increased levels of homocysteine. As a result, carriers of the A allele are at risk for neural tubes defects, vascular disease, stroke, migraine, depression, and infertility. Furthermore, individuals heterozygous for rs1801133 and rs1801131, another polymorphism in the MTHFR gene, have a more severe clinical phenotype that is similar to the AA genotype for rs1801133. Lastly, despite the prevalence of both minor alleles, the genotype combination rs1801131 GG and rs1801133 AA is nearly nonexistent in the population, suggesting it confers a significant genetic disadvantage.
MTRR rs1801394	The MTRR (5-methyltetrahydrofolate-homocysteine methyltransferase reductase) gene encodes an enzyme that regenerates methionine synthase, an enzyme encoded by the MTR gene, to a functional state. As a results, MTRR is also known as methionine synthase reductase, and it has a key role maintaining folate-methionine homeostasis. The polymorphism rs1801394 results in a methionine substitution for an isoleucine residue in the enzyme at position 22, and biochemical studies have found that the enzyme encoded by the G allele has a lower affinity for its target, methionine synthase, than the enzyme encoded by the A allele. These results suggest that carriers of the G allele, which produces a protein containing a methionine residue, may have reduced regeneration of methionine synthase and reduced conversion of homocysteine to methionine. Congruently, numerous studies have shown that G allele carriers have elevated homocysteine levels, which can be mediated by supplementation with folate. The G allele was also found to be a risk factor for neural tube defects and Down syndrome. Lastly, risk of neural tube defects was increased in G allele carriers who were also deficient in vitamin B12.
SLC19A1	The SLC19A1 (solute carrier family 19 member 1) gene encodes a folate transporter known as reduced folate carrier (RFC). RFC mediates cellular uptake of folate and folate derivatives, including antifolate pharmaceuticals. Folate is an essential nutrient that supplies a methyl group to support important biochemical functions, such as DNA synthesis and substrate methylation. For example, folate, with the help of vitamin B12, supplies the methyl group needed to convert homocysteine to methionine. The polymorphism rs1051266 results in an arginine substitution for a histidine residue in the transporter at position 27, which occurs in a transmembrane domain. Individuals with the CC genotype were found to have lower levels of plasma folate compared to individuals with the TT genotype, suggesting that the C allele, which encodes the arginine variant, produces a less efficient transporter. Additionally, individuals with the CC genotype for rs1051266 and the TT genotype for rs1801133, a variant in the MTHFR gene, were found to have higher levels of homocysteine. The C allele has been associated with delayed memory ability and increased susceptibility for neural tube defects. Lastly, carriers of the C allele may be less responsive to treatment with methotrexate, and individuals with the CC genotype may be at increased risk for ischemic stroke.
TCN1	The TCN1 (transcobalamin 1) gene encodes various isoforms of a carrier protein that binds vitamin B12 (cobalamin). The isoforms are differentially glycosylated, and they dimerize to form a vitamin B12-binding protein called haptocorrin. Haptocorrin protects vitamin B12 from the acidic environment of the stomach and transports it to the small intestine, where it can be bound by intrinsic factor. It is also estimated that haptocorrin carriers 70-80% of vitamin B12 in circulation. However, unlike transcobalamin encoded by the TCN2 gene, haptocorrin mainly delivers vitamin B12 to the liver. The polymorphism rs526934 occurs in the eighth intron, and carriers of the G allele have been shown to have lower vitamin B12 levels compared to individuals with the AA genotype.
TCN2	The TCN2 (transcobalamin 2) gene encodes a carrier protein that binds vitamin B12 (cobalamin) and delivers it to all tissues. Around 30% of circulating vitamin B12 is bound to TCN2. The polymorphism rs1801198 results in an arginine substitution for a proline residue in the protein at position 259, which occurs in the binding region for vitamin B12. In individuals with adequate vitamin B12 status, carriers of the G allele, which encodes an arginine residue, had less vitamin B12-bound TCN2 than C allele carriers. A large meta-analysis also reported that individuals with the GG genotype had significantly lower concentrations of vitamin B12-bound TCN2 and higher concentrations of homocysteine, a functional indicator of vitamin B12 status, compared to individuals with the CC genotype. Lastly, carriers of the C allele were shown to have lower levels of methylmalonic acid, which is converted to succinyl CoA in a vitamin B12-dependent reaction, suggesting that G allele carriers may have reduced levels of vitamin B12.
MITOCHONDRIA	The mitochondrial enzymes are responsible for energy production from the mitochondria. The mitochondria is known as the "powerhouse" of the cell and produces over 90% of the energy for a cell. The mitochondrial respiratory chain (also known as the electron transport chain) is where these 4 protein complexes are found. Polymorphic alterations in these enzymes reduce the energy output of the mitochondria and leads to symptoms of chronic fatigue, cognitive deficiency, exercise intolerance, low metabolic rate, muscle weakness, poor healing and higher rates of sleep disorders and mood abnormalities.

NQO1 rs1800566	The NQO1 (NAD(P)H quinone dehydrogenase 1) gene encodes a riboflavin-dependent enzyme that protects against oxidative stress. Moreover, it regenerates the antioxidant capacity of CoQ10 by reducing it. The polymorphism rs1800566 results in a serine substitution for a proline residue at position 187, which occurs in the FAD-binding site. The A allele, which encodes a serine residue, produces a variant with reduced stability due to reduced ability to bind FAD, a necessary co-factor. Because CoQ10 is sensitive to oxidative stress, molecular studies suggest that NOQ1 has a role in maintaining CoQ10 status, and a clinical study found an association with NOQ1 and CoQ10 status and response to supplementation. Lastly, molecular studies have found that NOQ1 function is also dependent on adequate levels of riboflavin.
PPARGC1A rs8192678	The PPARGC1A (PPARG coactivator 1 alpha) gene encodes a transcriptional coactivator, termed PGC-1?, that enhances mitochondrial biogenesis and function. PGC-1? activity leads to the transcription of TFAM, which translocates to the mitochondrial matrix where it stimulates mitochondrial DNA replication and expression of other mitochondrial gene needed for replication. The polymorphism rs8192678 results in a serine substitution for a glycine at position 487, and the T allele encodes a serine residue. Individuals with the TT genotype were found to have reduced mitochondrial DNA copy number, less endurance exercise capacity, and increased risk of metabolic dysfunction, suggesting that mitochondrial content is decreased. Additionally, carriers of the T allele may have increased risk of polycystic ovary syndrome (PCOS), which often coincides with metabolic dysfunction.
SIRT1 rs1467568	The SIRT1 (sirtuin 1) gene encodes a nicotinamide adenine dinucleotide (NAD+) and zinc-dependent histone deacetylase. SIRT1 is an important epigenetic regulator that responds to metabolic and oxidative stress to activate genes related to mitochondrial biogenesis and ATP production. SIRT1 activates PGC-1? through the SIRT1/PGC-1? axis, which responds to the cytosolic ratio of NAD+ to NADH. The polymorphism rs1467568 occurs in the eighth intron, and studies have found that G allele carriers may be at risk for increased BMI and obesity. Studies have also shown that SIRT1 expression was lower in overweight or obese individuals than it was in lean individuals. Together, these results suggest that G allele carriers may have reduced SIRT1 expression, restricting the SIRT1/PGC-1? axis and mitochondrial biogenesis. Furthermore, studies have found that physical activity and calorie restriction, known activators of SIRT1, can effectively address excess weight in G allele carriers. Lastly, BMI was noticeably higher in G allele carriers with low vitamin E, indicating that antioxidants may support SIRT1 and mitochondrial activity in G allele carriers as well.
TFAM rs1937	The TFAM (transcription factor A, mitochondrial) gene codes a transcription factor that promotes the expression of genes essential for mitochondrial DNA replication and repair. The polymorphism rs1937 results in a threonine substitution for a serine residue at position 12, which occurs in the mitochondrial signaling sequence. Individuals with the GG genotype were found to have reduced endurance exercise capacity and decreased longevity, suggesting that ability of the mitochondria to produce sufficient energy may be decreased. Furthermore, the GG genotype was associated with increased risk for Alzheimer disease.
NEUROTRANSMITTERS	Neurotransmitters are chemicals that are used to produce specific effects in the nervous system. These specific neurotransmitter genomics assess a person's risk for anxiety, depression and dysphoria.
COMT rs4680	The COMT (catechol-O-methyltransferase) gene encodes an enzyme that deactivates catecholamines, including neurotransmitters (adrenaline, noradrenaline and dopamine), by catalyzing the transfer of a methyl groups from S-adenosyl-methionine to a hydroxyl group on a catechol. Therefore, COMT has a crucial role in catecholamine neurotransmission and the metabolism of catechol hormones and xenobiotics. The polymorphism rs4860 results in a methionine substitution for a valine residue at position 108 for soluble COMT, which is prevalent in peripheral tissues, or position 158 for membrane-bound COMT, which is prevalent in the brain. The enzyme produced by the A allele, which encodes a methionine residue, reduces COMT activity due to thermal instability. Moreover, the A allele variant can have a three-to-fourfold reduction in enzyme activity compared to the G allele variant, and the A allele has been associated with a disadvantage processing aversive stimuli, reduced appetite, OCD, and anxiety. Furthermore, COMT metabolizes estrogen, and a study found that girls with the AA genotype had higher levels of free estradiol and earlier pubertal development than girls with the GG genotype, suggesting that the A allele may be associated with less efficient estrogen clearance. However, individuals with the GG genotype may have increased homocysteine levels when combined with a MTHFR variant.
GAD1 rs3828275	The GAD1 (Glutamic Acid Decarboxylase 1) gene encodes the rate-limiting enzyme responsible for conversion of glutamate, a stimulating neurotransmitter, to GABA, a calming neurotransmitter. A deficiency of GABA is associated with a variety of neuropsychological disorders, including anxiety, depression, and sleep disorders. The polymorphism, rs3828275, occurs in the third intron. Carriers of the minor allele have an increased risk for post-traumatic epilepsy, whereas carriers of the wild-type allele are potentially more responsive to treatment with SSRIs.
GAD1 rs769407	The GAD1 (Glutamic Acid Decarboxylase 1) gene encodes the rate-limiting enzyme responsible for conversion of glutamate, a stimulating neurotransmitter, to GABA, a calming neurotransmitter. A deficiency of GABA is associated with a variety of neuropsychological disorders, including anxiety, depression, and sleep disorders. The polymorphism, rs769407, occurs in the sixth intron and has a possible association with an increased risk of neuroticism and mood disorders. Additionally, it has been shown to associate with sleep disturbances in depressed patients.
MAOA	The MAOA (monoamine oxidase A) gene encodes for a riboflavin-dependent enzyme that degrades monoamine neurotransmitters, such as serotonin, dopamine, and norepinephrine. Thus, MAOA ends neuronal signaling induced by those neurotransmitters. MAOA is bound to the mitochondrial membrane by a transmembrane segment, and it has overlapping function with MAOB. However, MAOA has a higher affinity for serotonin and norepinephrine than MAOB. The G allele for the polymorphism rs6323 results in an enzyme with increased activity, and the G allele may be associated with attention deficit hyperactivity disorder (ADHD). Furthermore, women with the GG genotype had a sustained reaction to stressful stimuli, suggesting reduced stress resiliency.
MAOB	The MAOB (monoamine oxidase B) gene encodes for a riboflavin-dependent enzyme that degrades monoamine neurotransmitters, such as serotonin, dopamine, and norepinephrine. Thus, MAOB ends neuronal signaling induced by those neurotransmitters. MAOB is bound to the mitochondrial membrane by a transmembrane segment, and it has overlapping function with MAOA. However, MAOB has a higher affinity for dopamine, phenylethylamine, and benzylamine than MAOA. The polymorphism rs1799836 occurs in intron 13, and the T allele results in an enzyme with increased activity leading to a higher rate of dopamine turnover. As a result, the T allele has been associated with motor complications in Parkinson's disease, and the TT genotype may be a risk factor for Alzheimer's disease, which is known to present with decreased dopamine signaling. Lastly, survey data suggests that the T allele might be associated with feelings of stress, loneliness, sporadic attention, and anxiety.

Disclaimers

TESTING:

Testing Performed By: AC

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Testing for genetic variation/mutation on listed genes was performed using ProFlex PCR and Real-Time PCR with TaqMan® allele-specific probes on the QuantStudio 12K Flex. All genetic testing is performed by GX Sciences, LLC d/b/a Fagron Genomics US (“Fagron Genomics US”) (807 Las Cimas Pkwy, Suite 145, Austin, TX. 78746). This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Test results do not rule out the possibility that this individual could be a carrier of other mutations/variations not detected by this gene mutation/variation panel. Rare mutations surrounding these alleles may also affect our detection of genetic variations. Thus, the interpretation is given as a probability. Therefore, this genetic information shall be interpreted in conjunction with other clinical findings and familial history for the administration of specific nutrients. Patients should receive appropriate genetic counseling to explain the implications of these test results. Details of assay performance and algorithms leading to clinical recommendations are available upon request. The analytical and performance characteristics of this laboratory developed test (LDT) were determined by Fagron Genomics US’s laboratory (Laboratory Director: James Jacobson, PhD) pursuant to Clinical Laboratory Improvement Amendments (CLIA) requirements (CLIA #: 45D2144988).

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Fagron Genomics US SNP References

DETOXIFICATION SNP References

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