NutraCore

Lab Results

powered by GENOVA DIAGNOSTICS

# LAB RESULTS

Lab Results

NutraCore

BALANCE PROTOCOL

Patient:

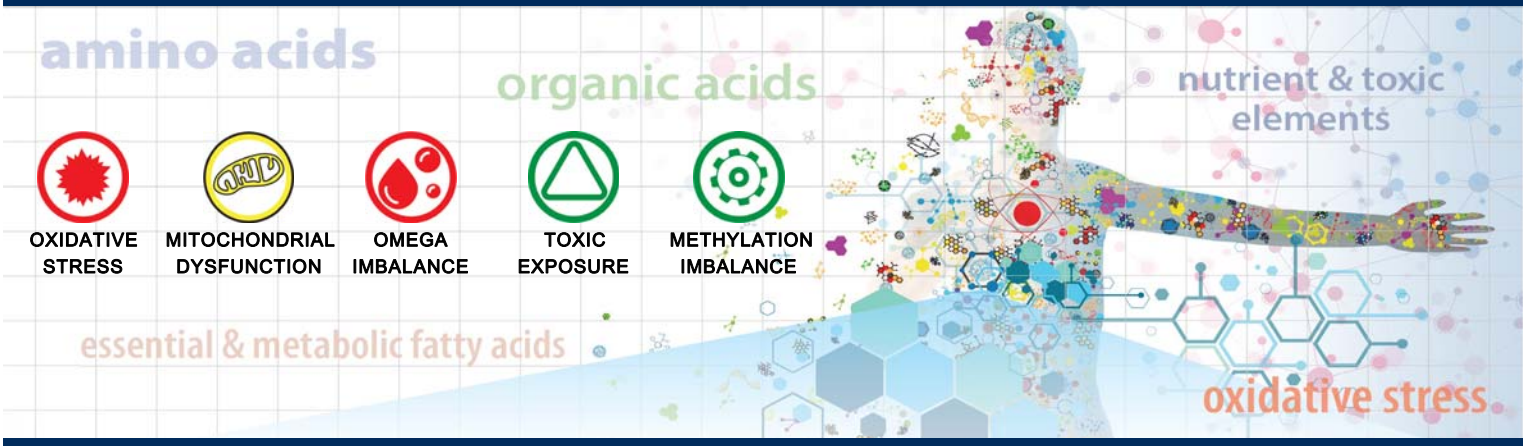
DOB: January 06, 1989
Sex: F
MRN:

**Order Number:**
Reported: July 02, 2026
Received: June 24, 2026
Collected: June 23, 2026

Balance Protocol Institute

## 3200 Metabolomix+ - FMV Urine

## Results Overview




## Functional Imbalance Scores

**Key** 0-4 : Minimal Need for Support | 5-7 : Moderate Need for Support | 8-10 : High Need for Support

### Need for Antioxidant Support

**Oxidative Stress**

8

| | |
|---|---|
| Cystine | ● |
| Cysteine | ● |
| Lipid Peroxides | ▲ |
| 8-OHdG | ● |
| Taurine | ▲ |
| Citric Acid | ▲ |
| cis-Aconitic Acid | △ |

### Need for Mitochondrial Support

**Mitochondrial Dysfunction**

5

| | |
|---|---|
| FIGLU | ● |
| Methylmalonic Acid | ● |
| Glutaric Acid | ● |
| Lactic Acid | △ |
| Pyruvic Acid | △ |
| Citric Acid | ▲ |
| cis-Aconitic Acid | △ |
| Isocitric Acid | △ |
| α-Ketoglutaric Acid | ▲ |
| Succinic Acid | △ |
| Malic Acid | △ |
| Adipic Acid | ● |
| Suberic Acid | ● |

### Need for Inflammation Support

**Omega Imbalance**

8

| | |
|---|---|
| Omega-3 Index | ▼ |
| Omega 6/3 Ratio | ● |
| α-Linolenic Acid | ▼ |
| Arachidonic Acid | ● |
| Linoleic Acid | ● |
| γ-Linolenic Acid | ● |
| Dihomo-γ-linolenic Acid | ▽ |

### Need for Reduced Exposure

**Toxic Exposure**

3

| | |
|---|---|
| Lead | ● |
| Mercury | ● |
| α-Hydroxyisobutyric Acid | ● |
| α-Ketophenylacetic Acid | ● |
| Arsenic | ● |
| Cadmium | ● |
| Pyroglutamic Acid | ● |
| Orotic Acid | ▲ |
| Citric Acid | ▲ |
| cis-Aconitic Acid | △ |
| Isocitric Acid | △ |
| Glutaric Acid | ● |

### Need for Methylation Support

**Methylation Imbalance**

4

| | |
|---|---|
| Methylmalonic Acid | ● |
| Methionine | ● |
| FIGLU | ● |
| Sarcosine | ▲ |
| Vanilmandelic Acid | ● |
| Arginine | ● |
| Glycine | ● |
| Serine | ▲ |
| Creatinine | ● |

# Nutrient Need Overview

| | Nutrient Need (0 1 2 3 4 5 6 7 8 9 10) | DRI | Suggested Recommendations | Provider Recommendations |
|---|---|---|---|---|
| **Antioxidants** | | | | |
| Vitamin A | | 2,333 IU | 5,000 IU | |
| Vitamin C | | 75 mg | 250 mg | |
| Vitamin E / Tocopherols | | 22 IU | 200 IU | |
| α-Lipoic Acid | | | 100 mg | |
| CoQ10 | | | 60 mg | |
| Glutathione | | | | |
| Plant-based Antioxidants | | | | |
| **B-Vitamins** | | | | |
| Thiamin - B1 | | 1.1 mg | 50 mg | |
| Riboflavin - B2 | | 1.1 mg | 25 mg | |
| Niacin - B3 | | 14 mg | 20 mg | |
| Pyridoxine - B6 | | 1.3 mg | 25 mg | |
| Biotin - B7 | | 30 mcg | 400 mcg | |
| Folate - B9 | | 400 mcg | 800 mcg | |
| Cobalamin - B12 | | 2.4 mcg | 100 mcg | |
| **Minerals** | | | | |
| Magnesium | | 320 mg | 800 mg | |
| Manganese | | 1.8 mg | 3.0 mg | |
| Molybdenum | | 45 mcg | 75 mcg | |
| Zinc | | 8 mg | 20 mg | |
| **Essential Fatty Acids** | | | | |
| Omega-3 Fatty Acids | | 500 mg | 2,000 mg | |
| **GI Support** | | | | |
| Digestive Support/Enzymes | | | 0 IU | |
| Microbiome Support/Probiotics | | | 10 billion CFU | |

## Amino Acids (mg/day)

| | | | |
|---|---|---|---|
| Arginine | 0 | Methionine | 0 |
| Asparagine | 0 | Phenylalanine | 0 |
| Cysteine | 0 | Serine | 0 |
| Glutamine | 0 | Taurine | 0 |
| Glycine | 0 | Threonine | 0 |
| Histidine | 0 | Tryptophan | 0 |
| Isoleucine | 0 | Tyrosine | 0 |
| Leucine | 0 | Valine | 0 |
| Lysine | 0 | | |

Recommendations for age and gender-specific supplementation are set by comparing levels of nutrient functional need to optimal levels as described in the peer-reviewed literature. They are provided as guidance for short-term support of nutritional deficiencies only.

Any application of the Nutrient Need Overview as a therapeutic intervention is to be determined by the ordering practitioner.

# Interpretation At-A-Glance

## Antioxidant Needs

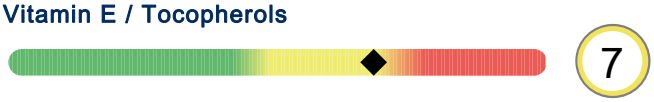
### Vitamin A


- Beta-carotene & other carotenoids are converted to vitamin A (retinol), involved in vision, antioxidant & immune function, gene expression & cell growth.
- Vitamin A deficiency may occur with chronic alcoholism, zinc deficiency, hypothyroidism, or oral contraceptives containing estrogen & progestin.
- Deficiency may result in night blindness, impaired immunity, healing & tissue regeneration, increased risk of infection, leukoplakia or keratosis.
- Food sources include cod liver oil, fortified cereals & milk, eggs, sweet potato, pumpkin, carrot, cantaloupe, mango, spinach, broccoli, kale & butternut squash.

### Vitamin C

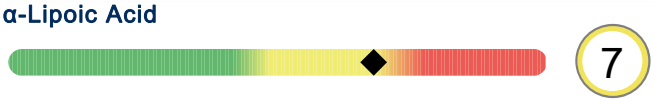

- Vitamin C is an antioxidant (also used in the regeneration of other antioxidants). It is involved in cholesterol metabolism, the production & function of WBCs and antibodies, and the synthesis of collagen, norepinephrine and carnitine.
- Deficiency may occur with oral contraceptives, aspirin, diuretics or NSAIDs.
- Deficiency can result in scurvy, swollen gingiva, periodontal destruction, loose teeth, sore mouth, soft tissue ulcerations, or increased risk of infection.
- Food sources include oranges, grapefruit, strawberries, tomato, sweet red pepper, broccoli and potato.

### Vitamin E / Tocopherols




- Alpha-tocopherol (body's main form of vitamin E) functions as an antioxidant, regulates cell signaling, influences immune function and inhibits coagulation.
- Deficiency may occur with malabsorption, cholestyramine, colestipol, isoniazid, orlistat, olestra and certain anti-convulsants (e.g., phenobarbital, phenytoin).
- Deficiency may result in peripheral neuropathy, ataxia, muscle weakness, retinopathy, and increased risk of CVD, prostate cancer and cataracts.
- Food sources include oils (olive, soy, corn, canola, safflower, sunflower), eggs, nuts, seeds, spinach, carrots, avocado, dark leafy greens and wheat germ.

### α-Lipoic Acid

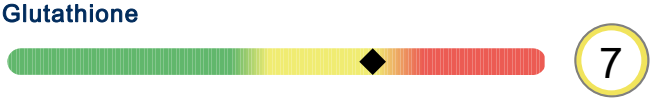



- α-Lipoic acid plays an important role in energy production, antioxidant activity (including the regeneration of vitamin C and glutathione), insulin signaling, cell signaling and the catabolism of α-keto acids and amino acids.
- High biotin intake can compete with lipoic acid for cell membrane entry.
- Optimal levels of α-lipoic acid may improve glucose utilization and protect against diabetic neuropathy, vascular disease and age-related cognitive decline.
- Main food sources include organ meats, spinach and broccoli. Lesser sources include tomato, peas, Brussels sprouts and brewer's yeast.

### CoQ10

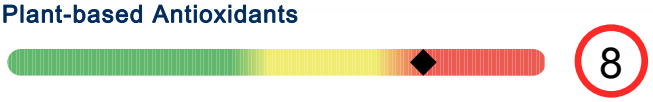

- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) or beta-blockers.
- Low levels may aggravate oxidative stress, diabetes, cancer, congestive heart failure, cardiac arrhythmias, gingivitis and neurologic diseases.
- Main food sources include meat, poultry, fish, soybean, canola oil, nuts and whole grains. Moderate sources include fruits, vegetables, eggs and dairy.

### Glutathione




- Glutathione (GSH) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and toxic exposure.
- Deficiency may result in oxidative stress & damage, impaired detoxification, altered immunity, macular degeneration and increased risk of chronic illness.
- Food sources of GSH precursors include meats, poultry, fish, soy, corn, nuts, seeds, wheat germ, milk and cheese.

### Plant-based Antioxidants




- Oxidative stress is the imbalance between the production of free radicals and the body's ability to readily detoxify these reactive species and/or repair the resulting damage with anti-oxidants.
- Oxidative stress can be endogenous (energy production and inflammation) or exogenous (exercise, exposure to environmental toxins).
- Oxidative stress has been implicated clinically in the development of neurodegenerative diseases, cardiovascular diseases and chronic fatigue syndrome.
- Antioxidants may be found in whole food sources (e.g., brightly colored fruits & vegetables, green tea, turmeric) as well as nutraceuticals (e.g., resveratrol, EGCG, lutein, lycopene, ginkgo, milk thistle, etc.).

## KEY

Function of Nutrient | Cause of Deficiency | Complications of Deficiency | Food Sources of Nutrient

# Interpretation At-A-Glance

## B-Vitamin Needs

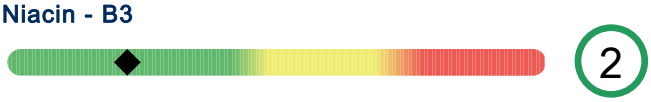
### Thiamin - B1


- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency may lead to dry beriberi (e.g., neuropathy, muscle weakness), wet beriberi (e.g., cardiac problems, edema), encephalopathy or dementia.
- Food sources include lentils, whole grains, wheat germ, Brazil nuts, peas, organ meats, brewer's yeast, blackstrap molasses, spinach, milk & eggs.

### Riboflavin - B2


- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.
- B2 deficiency may result in oxidative stress, mitochondrial dysfunction, low uric acid, low B3 or B6, high homocysteine, anemia or oral & throat inflammation.
- Food sources include milk, cheese, eggs, whole grains, beef, chicken, wheat germ, fish, broccoli, asparagus, spinach, mushrooms and almonds.

### Niacin - B3




- B3 is used to form NAD and NADP, involved in energy production from food, fatty acid & cholesterol synthesis, cell signaling, DNA repair & cell differentiation.
- Low B3 may result from deficiencies of tryptophan (B3 precursor), B6, B2 or Fe (cofactors in B3 production), or from long-term isoniazid or oral contraceptive use.
- B3 deficiency may result in pellagra (dermatitis, diarrhea, dementia), neurologic symptoms (e.g., depression, memory loss), bright red tongue or fatigue.
- Food sources include poultry, beef, organ meats, fish, whole grains, peanuts, seeds, lentils, brewer's yeast and lima beans.

### Pyridoxine - B6


- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or digoxin.
- B6 deficiency may result in neurologic symptoms (e.g., irritability, depression, seizures), oral inflammation, impaired immunity or increased homocysteine.
- Food sources include poultry, beef, beef liver, fish, whole grains, wheat germ, soybean, lentils, nuts & seeds, potato, spinach and carrots.

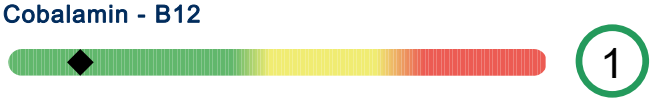
### Biotin - B7


- Biotin is a cofactor for enzymes involved in functions such as fatty acid synthesis, mitochondrial FA oxidation, gluconeogenesis and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN, anticonvulsants, high-dose B5, sulfa drugs & other antibiotics.
- Low levels may result in neurologic symptoms (e.g., paresthesias, depression), hair loss, scaly rash on face or genitals or impaired immunity.
- Food sources include yeast, whole grains, wheat germ, eggs, cheese, liver, meats, fish, wheat, nuts & seeds, avocado, raspberries, sweet potato and cauliflower.

### Folate - B9


- Folate plays a key role in coenzymes involved in DNA and SAMe synthesis, methylation, nucleic acids & amino acid metabolism and RBC production.
- Low folate may result from alcoholism, high-dose NSAIDs, diabetic meds, H2 blockers, some diuretics and anti-convulsants, SSRIs, methotrexate, trimethoprim, pyrimethamine, triamterene, sulfasalazine or cholestyramine.
- Folate deficiency can result in anemia, fatigue, low methionine, increased homocysteine, impaired immunity, heart disease, birth defects and CA risk.
- Food sources include fortified grains, green vegetables, beans & legumes.

### Cobalamin - B12




- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 blockers, PPIs), vegan diets, diabetic meds, cholestyramine, chloramphenicol, neomycin or colchicine.
- B12 deficiency can lead to anemia, fatigue, neurologic symptoms (e.g., paresthesias, memory loss, depression, dementia), methylation defects or chromosome breaks.
- Food sources include shellfish, red meat, poultry, fish, eggs, milk and cheese.

## KEY

Function of Nutrient | Cause of Deficiency | Complications of Deficiency | Food Sources of Nutrient

# Interpretation At-A-Glance

## Mineral Needs

### Magnesium


- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses of zinc.
- Low Mg may result in muscle weakness/spasm, constipation, depression, hypertension, arrhythmias, hypocalcemia, hypokalemia or personality changes.
- Food sources include dark leafy greens, oatmeal, buckwheat, unpolished grains, chocolate, milk, nuts & seeds, lima beans and molasses.

### Manganese


- Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production and digestion.
- Impaired absorption of Mn may occur with excess intake of Fe, Ca, Cu, folic acid, or phosphorous compounds, or use of long-term TPN, Mg-containing antacids or laxatives.
- Deficiency may result in impaired bone/connective tissue growth, glucose & lipid dysregulation, infertility, oxidative stress, inflammation or hyperammonemia.
- Food sources include whole grains, legumes, dried fruits, nuts, dark green leafy vegetables, liver, kidney and tea.

### Molybdenum

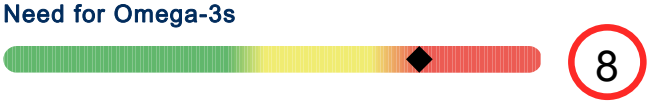

- Molybdenum is a cofactor for enzymes that convert sulfites to sulfate, and nucleotides to uric acid, and that help metabolize aldehydes & other toxins.
- Low Mo levels may result from long-term TPN that does not include Mo.
- Mo deficiency may result in increased sulfite, decreased plasma uric acid (and antioxidant function), deficient sulfate, impaired sulfation (detoxification), neurologic disorders or brain damage (if severe deficiency).
- Food sources include buckwheat, beans, grains, nuts, beans, lentils, meats and vegetables (although Mo content of plants depends on soil content).

### Zinc


- Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion and antioxidant function.
- Low levels may occur with malabsorption, alcoholism, chronic diarrhea, diabetes, excess Cu or Fe, diuretics, ACE inhibitors, H2 blockers or digoxin.
- Deficiency can result in hair loss and skin rashes, also impairments in growth & healing, immunity, sexual function, taste & smell and digestion.
- Food sources include oysters, organ meats, soybean, wheat germ, seeds, nuts, red meat, chicken, herring, milk, yeast, leafy and root vegetables.

## Essential Fatty Acid Needs

### Need for Omega-3s




- Omega-3 (O3) and Omega-6 (O6) fatty acids are polyunsaturated fatty acids that cannot be synthesized by the human body. They are classified as essential nutrients and must be obtained from dietary sources.
- The standard American diet is much higher in O6 than O3 fatty acids. Deficiency of EFAs may result from poor dietary intake and/or poor conversion from food sources.
- EFA deficiency is associated with decreased growth & development of infants and children, dry skin/rash, poor wound healing, and increased risk of infection, cardiovascular and inflammatory diseases.
- Dietary sources of the O6 Linoleic Acid (LA) include vegetable oils, nuts, seeds and some vegetables. Dietary sources of the O3 a-Linolenic Acid (ALA) include flaxseeds, walnuts, and their oils. Fish (mackerel, salmon, sardines) are the major dietary sources of the O3 fatty acids EPA and DHA.

## KEY

Function of Nutrient | Cause of Deficiency | Complications of Deficiency | Food Sources of Nutrient

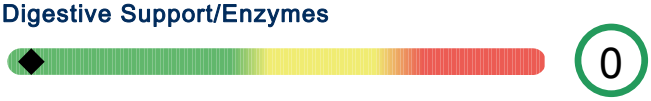
# Interpretation At-A-Glance

## Microbiome & Digestive Support

### Microbiome Support/Probiotics


- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhance digestion & absorption; decrease severity of diarrheal illness; modulate of immune function & intestinal permeability.
- Alterations of gastrointestinal microflora may result from C-section delivery, antibiotic use, improved sanitation, decreased consumption of fermented foods and use of certain drugs.
- Some of the diseases associated with microflora imbalances include: IBS, IBD, fibromyalgia, chronic fatigue syndrome, obesity, atopic illness, colic and cancer.
- Food sources rich in probiotics are yogurt, kefir and fermented foods.

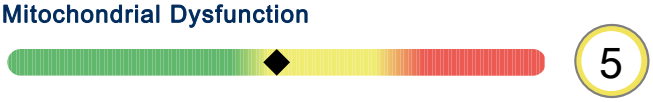
### Digestive Support/Enzymes




- Pancreatic enzymes are secreted by the exocrine glands of the pancreas and include protease/peptidase, lipase and amylase.
- Pancreatic exocrine insufficiency may be primary or secondary in nature. Any indication of insufficiency warrants further evaluation for underlying cause (i.e., celiac disease, small intestine villous atrophy, small bowel bacterial overgrowth).
- A high functional need for digestive enzymes suggests that there is an impairment related to digestive capacity.
- Determining the strength of the pancreatic enzyme support depends on the degree of functional impairment. Supplement potency is based on the lipase units present in both prescriptive and non-prescriptive agents.

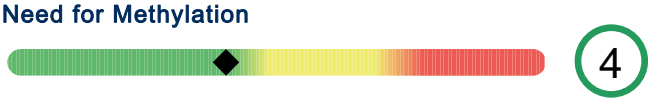
## Functional Imbalances

### Mitochondrial Dysfunction



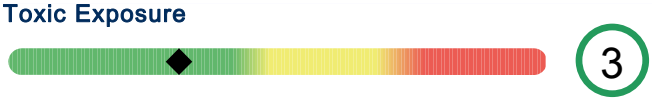

- Mitochondria are a primary site of generation of reactive oxygen species. Oxidative damage is considered an important factor in decline of physiologic function that occurs with aging and stress.
- Mitochondrial defects have been identified in cardiovascular disease, fatigue syndromes, neurologic disorders such as Parkinson's and Alzheimer's disease, as well as a variety of genetic conditions. Common nutritional deficiencies can impair mitochondrial efficiency.

### Need for Methylation




- Methylation is an enzymatic process that is critical for both synthesis and inactivation. DNA, estrogen and neurotransmitter metabolism are all dependent on appropriate methylation activity.
- B vitamins and other nutrients (methionine, magnesium, selenium) functionally support catechol-O-methyltransferase (COMT), the enzyme responsible for methylation.

### Toxic Exposure

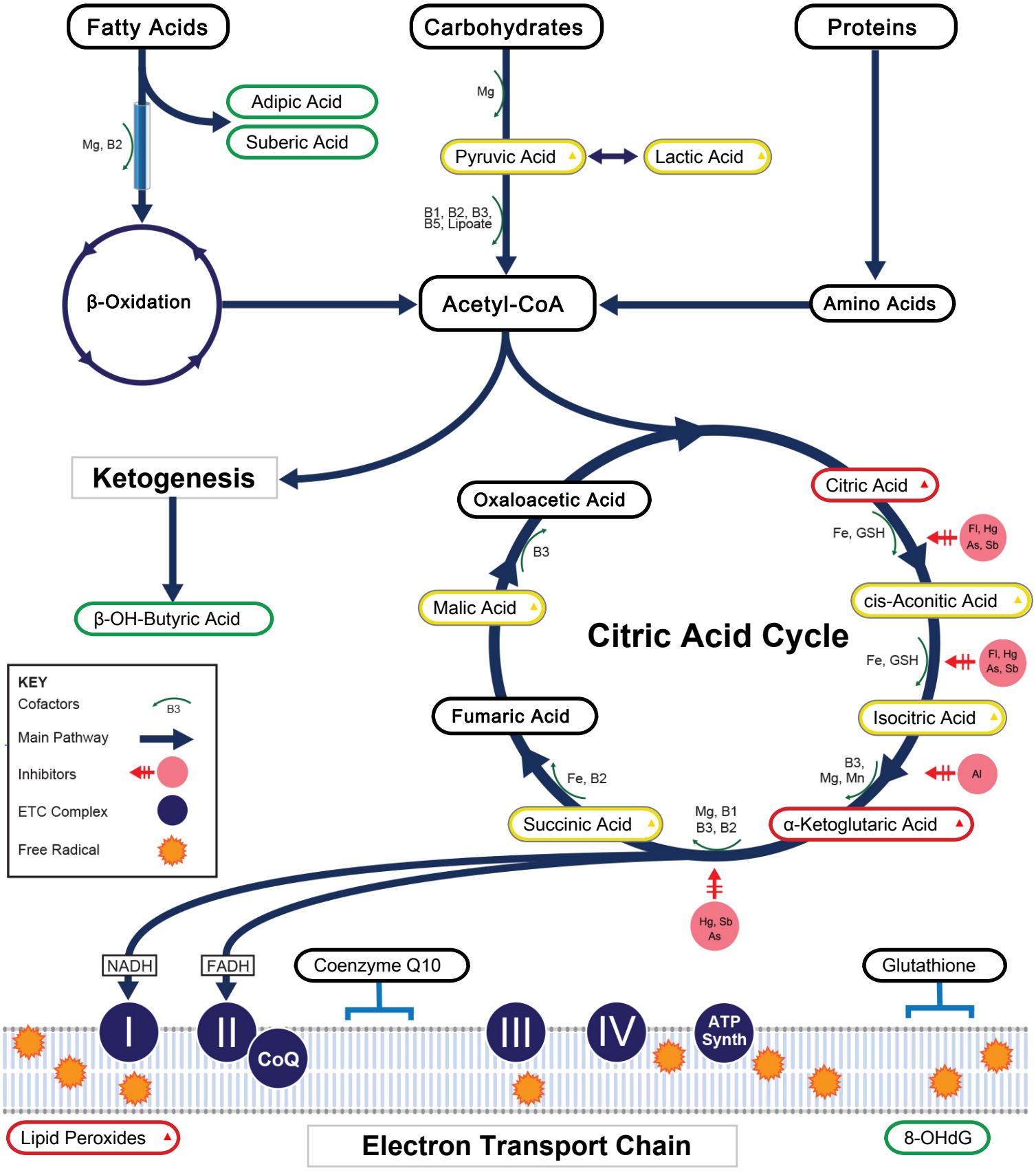



- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal studies suggest that drinking MTBE may cause gastrointestinal irritation, liver and kidney damage and nervous system effects.
- Styrene is classified by the US EPA as a "potential human carcinogen," and is found widely distributed in commercial products such as rubber, plastic, insulation, fiberglass, pipes, food containers and carpet backing.
- Levels of these toxic substances should be examined within the context of the body's functional capacity for methylation and need for glutathione.

## KEY

Function of Nutrient | Cause of Deficiency | Complications of Deficiency | Food Sources of Nutrient

# Oxidative Stress & Mitochondrial Dysfunction



All biomarkers reported in mmol/mol creatinine unless otherwise noted.

# Organic Acids

## Malabsorption & Dysbiosis Markers

### Malabsorption Markers

| | | Reference Range |
|---|---|---|
| Indoleacetic Acid | 2.0 | <= 4.2 |
| Phenylacetic Acid | 0.09 | <= 0.12 |

### Dysbiosis Markers

| | | Reference Range |
|---|---|---|
| Dihydroxyphenylpropionic Acid (DHPPA) | 0.4 | <= 5.3 |
| 3-Hydroxyphenylacetic Acid | 2.0 | <= 8.1 |
| 4-Hydroxyphenylacetic Acid | 12 | <= 29 |
| Benzoic Acid | 0.32 | <= 0.05 |
| Hippuric Acid | 84 | <= 603 |

### Yeast / Fungal Dysbiosis Markers

| | | Reference Range |
|---|---|---|
| D-Arabinitol | 18 | <= 36 |
| Citramalic Acid | 1.8 | <= 5.8 |
| Tartaric Acid | 11 | <= 15 |

## Vitamin Markers

### Branched-Chain Catabolites (B1, B2, B3, ALA)

| | | Reference Range |
|---|---|---|
| α-Ketoadipic Acid | 1.0 | <= 1.7 |
| α-Ketoisovaleric Acid | 0.52 | <= 0.97 |
| α-Ketoisocaproic Acid | 0.57 | <= 0.89 |
| α-Keto-β-Methylvaleric Acid | 1.8 | <= 2.1 |
| Glutaric Acid | 0.29 | <= 0.51 |
| Isovalerylglycine | 2.1 | <= 3.7 |

### Methylation Markers (Folate, B12)

| | | Reference Range |
|---|---|---|
| Formiminoglutamic Acid (FIGlu) | 0.6 | <= 1.5 |
| Methylmalonic Acid | 0.7 | <= 1.9 |

### Biotin Markers

| | | Reference Range |
|---|---|---|
| 3-Hydroxypropionic Acid | 11 | 5-22 |
| 3-Hydroxyisovaleric Acid | 33 | <= 29 |

## Cellular Energy & Mitochondrial Markers

### Fatty Acid Metabolism

| | | Reference Range |
|---|---|---|
| Adipic Acid | 1.3 | <= 2.8 |
| Suberic Acid | 1.0 | <= 2.1 |

### Carbohydrate Metabolism

| | | Reference Range |
|---|---|---|
| Pyruvic Acid | 23 | 7-32 |
| Lactic Acid | 14.3 | 1.9-19.8 |
| α-Hydroxybutyric Acid | 0.82 | <= 0.83 |
| β-OH-Butyric Acid | 1.6 | <= 2.8 |
| β-OH-β-Methylglutaric Acid | 6 | <= 15 |

### Energy Metabolism

| | | Reference Range |
|---|---|---|
| Citric Acid | 782 | 40-520 |
| cis-Aconitic Acid | 28 | 10-36 |
| Isocitric Acid | 59 | 22-65 |
| α-Ketoglutaric Acid | 63 | 4-52 |
| Succinic Acid | 3.2 | 0.4-4.6 |
| Malic Acid | 3.0 | <= 3.0 |

## Neurotransmitter Metabolites

### Kynurenine Markers (Vitamin B6)

| | | Reference Range |
|---|---|---|
| Kynurenic Acid | 2.8 | <= 7.1 |
| Quinolinic Acid | 8.8 | <= 9.1 |
| Kynurenic / Quinolinic Ratio | 0.32 | >= 0.44 |
| Xanthurenic Acid | 0.76 | <= 0.96 |

### Catecholamine Markers

| | | Reference Range |
|---|---|---|
| Homovanillic Acid | 2.0 | 1.2-5.3 |
| Vanilmandelic Acid | 1.5 | 0.4-3.6 |
| 3-Methyl-4-OH-phenylglycol | 0.11 | 0.02-0.22 |

### Serotonin Markers

| | | Reference Range |
|---|---|---|
| 5-OH-indoleacetic Acid | 6.8 | 3.8-12.1 |

## Toxin & Detoxification Markers

| | | Reference Range |
|---|---|---|
| Pyroglutamic Acid | 27 | 16-34 |
| α-Ketophenylacetic Acid (from Styrene) | 0.16 | <= 0.46 |
| α-Hydroxyisobutyric Acid (from MTBE) | 4.8 | <= 6.7 |
| Orotic Acid | 1.58 | 0.33-1.01 |

Methodology: GCMS, LC/MS/MS, Alkaline Picrate, Colorimetric

Organic Acid Reference Ranges are Age Specific

Methodology: Colorimetric, thiobarbituric acid reactive substances (TBARS), Alkaline Picrate, Hexokinase/G-6-PDH, HPLC, GC/MS

## Organic Acids

### Oxalate Markers

| | | Reference Range |
|---|---|---|
| Glyceric Acid | 9.2 | 3.5-16.4 |
| Glycolic Acid | 56 | <= 67 |
| Oxalic Acid | 32 | <= 78 |

All biomarkers reported in mmol/mol creatinine.

### Creatinine Concentration

| | | Reference Range |
|---|---|---|
| Urine Creatinine ◆ | 13.2 | 3.1-19.5 mmol/L |

## Oxidative Stress Markers

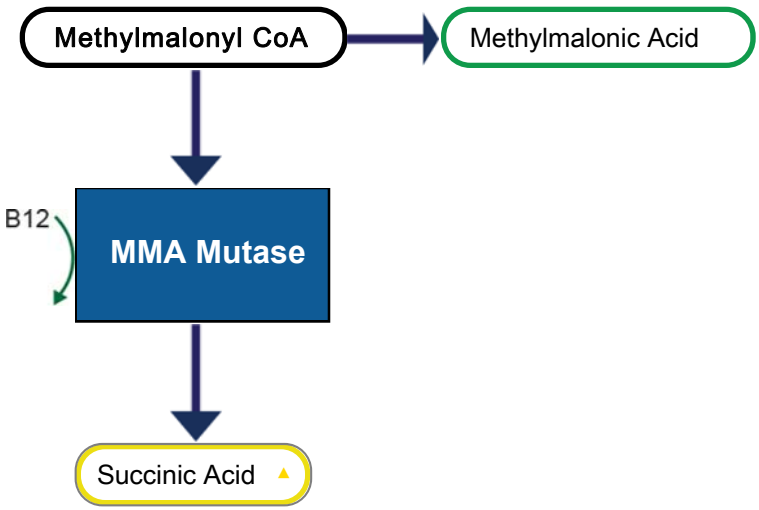
### Oxidative Damage

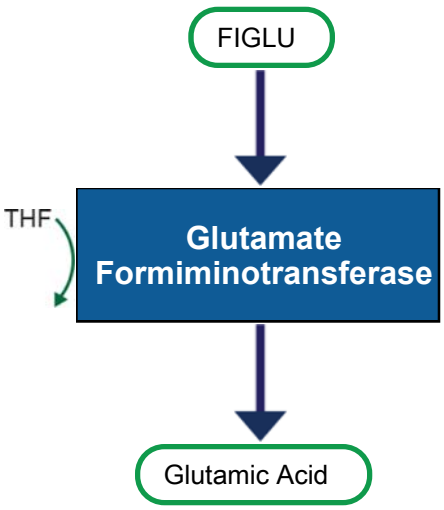
| | | Reference Range |
|---|---|---|
| Lipid Peroxides (urine) | 11.5 | <= 10.0 micromol/g Creat. |
| 8-OHdG (urine) | 5 | <= 15 mcg/g Creat. |

The Oxidative Stress reference ranges are based on an adult population.

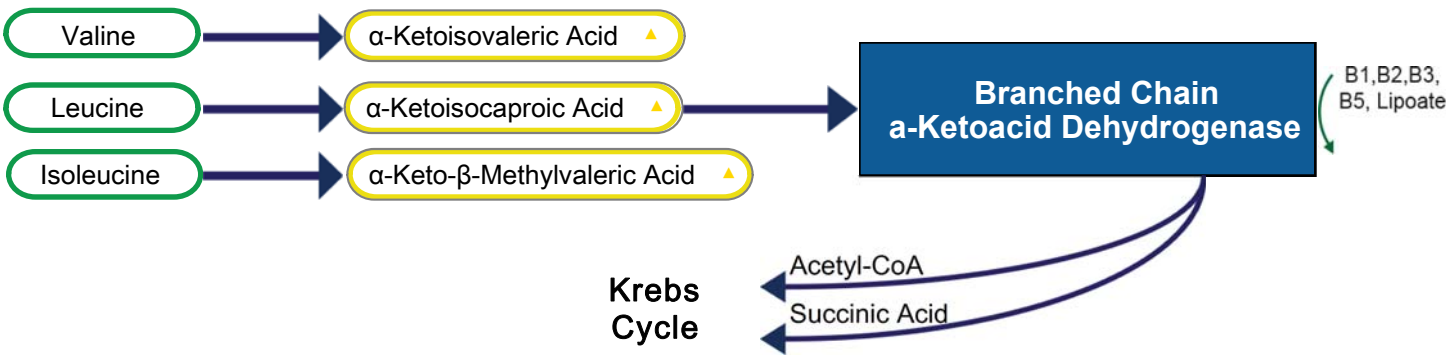
## Pathways

### Methylation Markers




### Branched-Chain Amino Acid Metabolism



All biomarkers reported in micromol/g creatinine unless otherwise noted.

# Amino Acids (FMV)

## Nutritionally Essential Amino Acids

| Amino Acid | | Reference Range |
|---|---|---|
| Arginine | 10 | 3-33 |
| Histidine | 622 | 127-800 |
| Isoleucine | 9 | 3-28 |
| Leucine | 15 | 4-46 |
| Lysine | 50 | 11-175 |
| Methionine | 7 | 2-18 |
| Phenylalanine | 39 | 8-71 |
| Taurine | >UL | 21-424 |
| Threonine | 74 | 12-123 |
| Tryptophan | 46 | 5-53 |
| Valine | 23 | 7-49 |

## Nonessential Protein Amino Acids

| Amino Acid | | Reference Range |
|---|---|---|
| Alanine | 258 | 63-295 |
| Asparagine | 87 | 25-119 |
| Aspartic Acid | 17 | <= 14 |
| Cysteine | 30 | 8-74 |
| Cystine | 26 | 10-104 |
| γ-Aminobutyric Acid | 2 | <= 5 |
| Glutamic Acid | 15 | 4-27 |
| Glutamine | 500 | 110-528 |
| Proline | 6 | 1-13 |
| Tyrosine | 69 | 11-135 |

## Creatinine Concentration

| | | Reference Range |
|---|---|---|
| Urine Creatinine ◆ | 12.7 | 3.1-19.5 mmol/L |

Amino Acid reference ranges are age specific.

Methodology: LC/MS/MS, Alkaline Picrate

## Intermediary Metabolites

### B-Vitamin Markers

| | | Reference Range |
|---|---|---|
| α-Aminoadipic Acid | 23 | 2-47 |
| α-Amino-N-butyric Acid | 11 | 2-25 |
| β-Aminoisobutyric Acid | 12 | 11-160 |
| Cystathionine | 16 | 2-68 |

### Urea Cycle Markers

| | | |
|---|---|---|
| Citrulline | 2.8 | 0.6-3.9 |
| Ornithine | 6 | 2-21 |
| Urea ◆ | 237 | 168-465 mmol/g creatinine |

### Glycine/Serine Metabolites

| | | |
|---|---|---|
| Glycine | 469 | 95-683 |
| Serine | 176 | 40-163 |
| Ethanolamine | 91 | 50-235 |
| Phosphoethanolamine | 3 | 1-13 |
| Phosphoserine | 13 | <= 13 |
| Sarcosine | 2.2 | <= 1.2 |

## Dietary Peptide Related Markers

| | | Reference Range |
|---|---|---|
| Anserine (dipeptide) | 1.7 | 0.4-105.1 |
| Carnosine (dipeptide) | 8 | 1-28 |
| 1-Methylhistidine | 239 | 38-988 |
| 3-Methylhistidine | 169 | 44-281 |
| β-Alanine | 6 | <= 22 |

# 3202 Add-on Bloodspot Essential & Metabolic Fatty Acids – Bloodspot

Methodology: GCMS

## Essential & Metabolic Fatty Acids (Bloodspot)

### Omega-3 Fatty Acids

| Analyte | | Reference Range |
|---|---|---|
| | (cold water fish, flax, walnut) | |
| α-Linolenic (ALA) 18:3 n3 | 0.22 | >= 0.28 wt % |
| Eicosapentaenoic (EPA) 20:5 n3 | 0.19 | >= 0.12 wt % |
| Docosapentaenoic (DPA) 22:5 n3 | 0.63 | >= 0.34 wt % |
| Docosahexaenoic (DHA) 22:6 n3 | 1.0 | >= 0.8 wt % |
| **% Omega-3s** | 2.1 | >= 1.6 |

### Omega-9 Fatty Acids

| Analyte | | Reference Range |
|---|---|---|
| | (olive oil) | |
| Oleic 18:1 n9 | 17 | 14-21 wt % |
| Nervonic 24:1 n9 | 1.9 | 1.1-1.8 wt % |
| **% Omega-9s** | 18.7 | 17.3-22.5 |

### Saturated Fatty Acids

| Analyte | | Reference Range |
|---|---|---|
| | (meat, dairy, coconuts, palm oils) | |
| Palmitic C16:0 | 23 | 19-27 wt % |
| Stearic C18:0 | 13 | 9-12 wt % |
| Arachidic C20:0 | 0.31 | 0.24-0.40 wt % |
| Behenic C22:0 | 0.79 | 0.88-1.61 wt % |
| Tricosanoic C23:0 | 0.25 | 0.19-0.26 wt % |
| Lignoceric C24:0 | 1.4 | 1.1-1.9 wt % |
| Pentadecanoic C15:0 | 0.16 | 0.14-0.30 wt % |
| Margaric C17:0 | 0.33 | 0.24-0.45 wt % |
| **% Saturated Fats** | 39.1 | 39.8-43.6 |

### Omega-6 Fatty Acids

| Analyte | | Reference Range |
|---|---|---|
| | (vegetable oil, grains, most meats, dairy) | |
| Linoleic (LA) 18:2 n6 | 24.7 | 18.8-28.3 wt % |
| γ-Linolenic (GLA) 18:3 n6 | 0.20 | 0.15-0.54 wt % |
| Dihomo-γ-linolenic (DGLA) 20:3 n6 | 1.15 | >= 1.02 wt % |
| Arachidonic (AA) 20:4 n6 | 10 | 7-12 wt % |
| Docosatetraenoic (DTA) 22:4 n6 | 1.50 | 0.45-1.25 wt % |
| Eicosadienoic 20:2 n6 | 0.30 | <= 0.26 wt % |
| **% Omega-6s** | 38.1 | 30.5-39.7 |

### Monounsaturated Fatty Acids

#### Omega-7 Fatty Acids

| Analyte | | Reference Range |
|---|---|---|
| Palmitoleic 16:1 n7 | 0.59 | <= 2.58 wt % |
| Vaccenic 18:1 n7 | 1.15 | <= 1.65 wt % |

#### Trans Fats

| Analyte | | Reference Range |
|---|---|---|
| Elaidic 18:1 n9t | 0.35 | <= 0.59 wt % |

### Delta-6-Desaturase Activity

| Analyte | | Reference Range |
|---|---|---|
| | Upregulated Functional Impaired | |
| Linoleic / DGLA 18:2 n6 / 20:3 n6 | 21.4 | 12.6-31.5 |

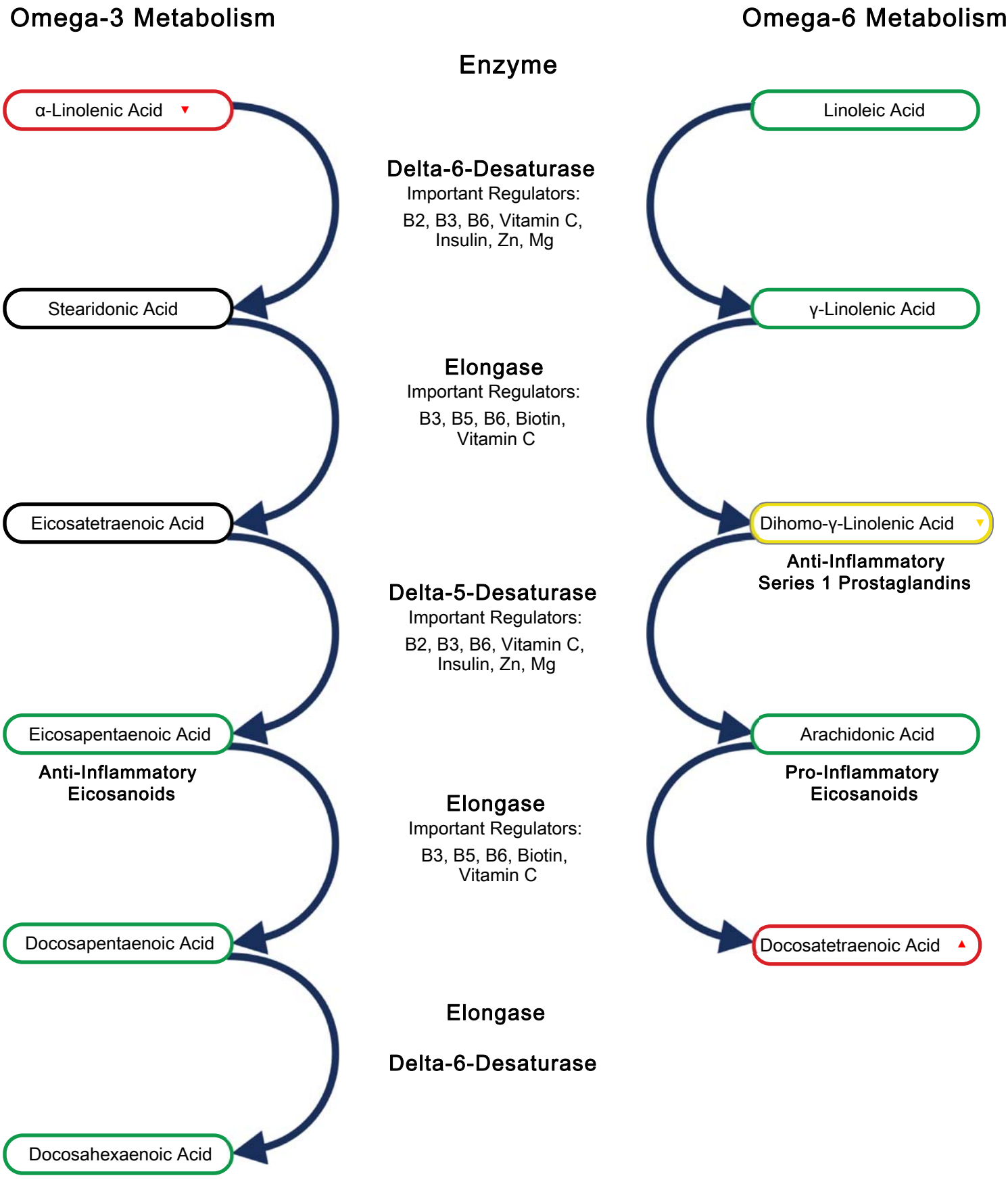
### Cardiovascular Risk

| Analyte | | Reference Range |
|---|---|---|
| Omega-6s / Omega-3s | 18.5 | 8.5-27.4 |
| AA / EPA 20:4 n6 / 20:5 n3 | 54 | 10-86 |
| Omega-3 Index | 3.2 | >= 4.0 |

The Essential Fatty Acid reference ranges are based on an adult population.

* The patient results for the Omega 3 Index have been converted to red blood cell equivalence in order to maintain applicability to the literature-based reference ranges for this marker.

# Fatty Acid Metabolism



## 3204 Add - on Comprehensive Urine Elements - FMV Urine

*Methodology: ICP-MS and Alkaline Picrate*

# Elemental Markers

## Toxic Elements

| Element | Results in µg/g creatinine | Reference Range |
|---|---|---|
| Lead | 0.2 | <= 1.4 |
| Mercury | 0.12 | <= 2.19 |
| Aluminum | 4.8 | <= 22.3 |
| Antimony | 0.045 | <= 0.149 |
| Arsenic | 2 | <= 50 |
| Barium | 2.8 | <= 6.7 |
| Bismuth | 0.00 | <= 2.28 |
| Cadmium | 0.06 | <= 0.64 |
| Cesium | 1.9 | <= 10.5 |
| Gadolinium | <dl | <= 0.019 |
| Gallium | <dl | <= 0.028 |
| Nickel | 1.33 | <= 3.88 |
| Platinum | <dl | <= 0.033 |
| Rubidium | 177 | <= 2,263 |
| Thallium | 0.042 | <= 0.298 |
| Tin | 0.26 | <= 2.04 |
| Tungsten | 0.110 | <= 0.211 |
| Uranium | 0.008 | <= 0.026 |

## Nutrient Elements

| Element | Results in µg/g creatinine | Reference Range |
|---|---|---|
| Chromium | <dl | 0.6-9.4 |
| Cobalt | 0.10 | 0.01-2.60 |
| Copper | 5.6 | 4.0-11.4 |
| Iron | 4 | 5-64 |
| Lithium | 16 | 9-129 |
| Manganese | 0.07 | 0.03-1.16 |
| Molybdenum | 68 | 15-175 |
| Selenium | 35 | 32-333 |
| Strontium | 141 | 47-346 |
| Vanadium | 0.1 | 0.1-3.2 |
| Zinc | 440 | 63-688 |

| Element | Results in mg/g creatinine | Reference Range |
|---|---|---|
| Calcium (urine quantitative, timed specimen) | 237 | 37-313 |
| Magnesium | 94 | 41-267 |
| Sulfur | 584 | 367-1,328 |

## Creatinine Concentration

| | | Reference Range |
|---|---|---|
| Urine Creatinine ◆ | 151 | 23-205 mg/dL |

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ◆, the assays have not been cleared by the U.S. Food and Drug Administration.

NutraCore

BALANCE PROTOCOL

Patient:

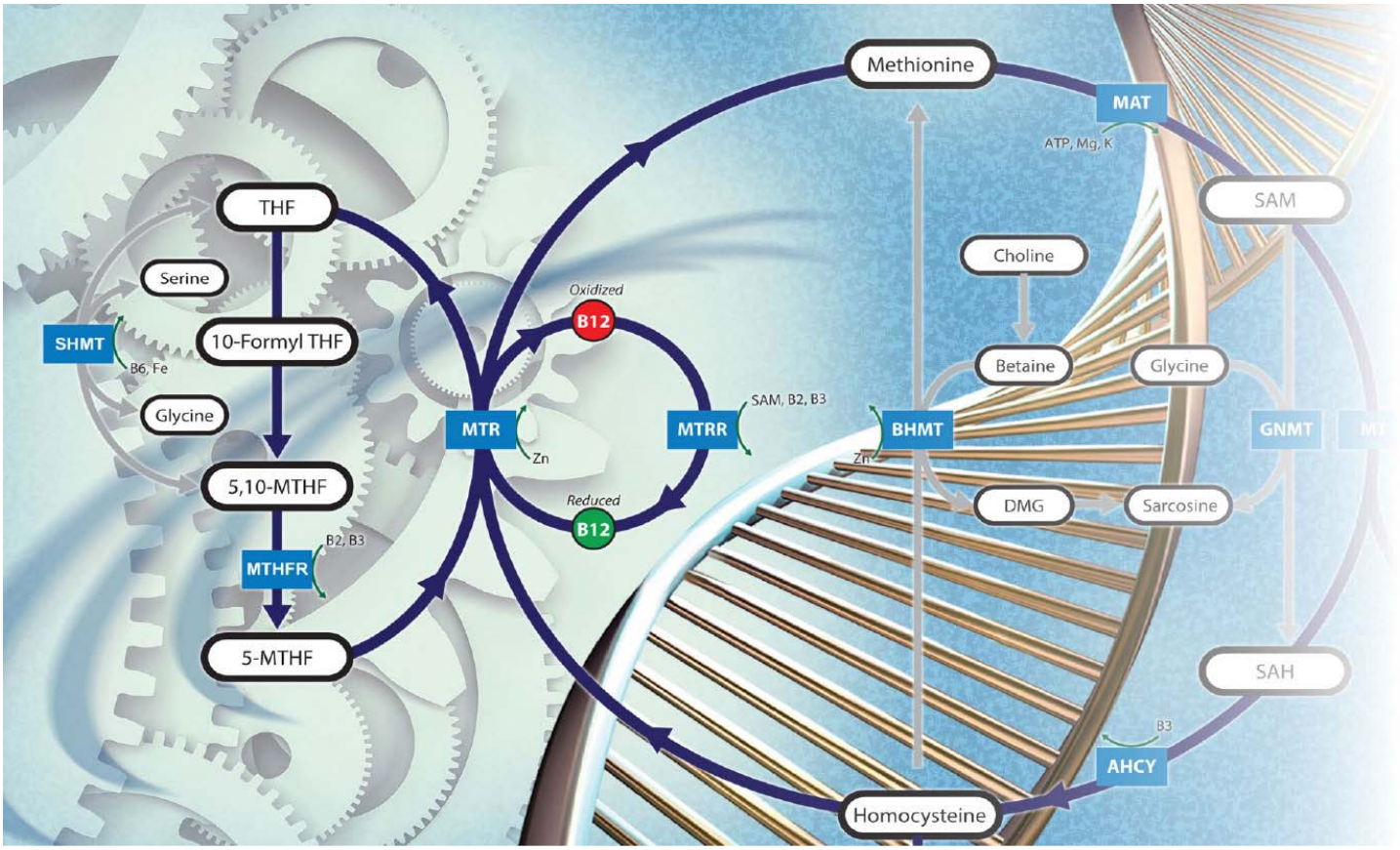
DOB: January 06, 1989
Sex: F
MRN:

**Order Number:**
Reported: June 30, 2026
Received: June 24, 2026
Collected: June 23, 2026

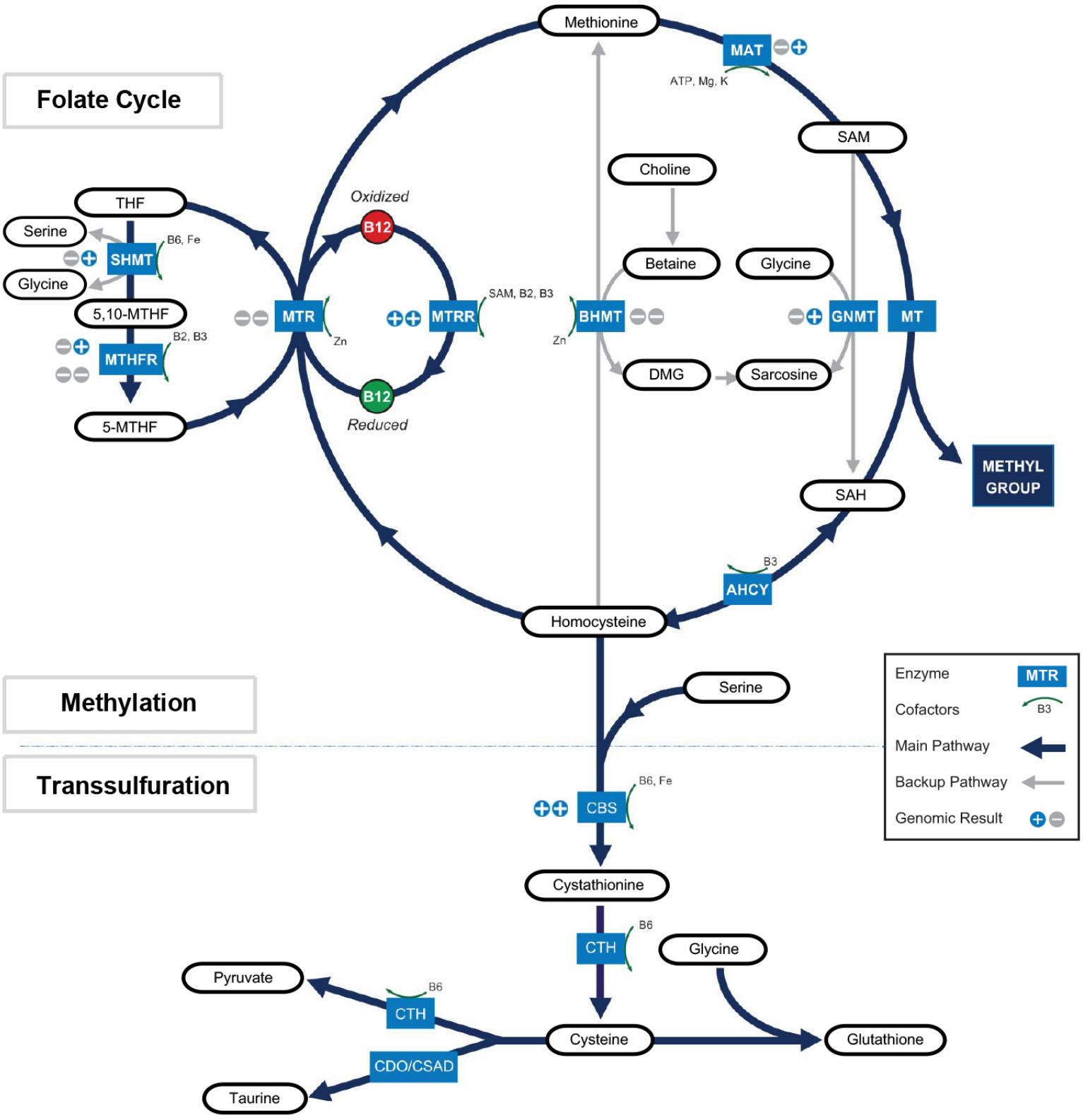
Balance Protocol Institute

## **3542 Methylation Genomics** - Buccal Swab

*Methodology: PCR Sequencing*



## Methylation / Transsulfuration Pathway




*Energy Production*

*Detoxification*

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## BHMT G742A

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| G | G |
| Wild Type - | Wild Type - |

Potential Impact:

**No Upregulation**

| Genotypes | Amino Acid |
|---|---|
| G G | Arg Arg |
| G A | Arg Gln |
| A A | Gln Gln |

**Amino Acid Position:** 239

***Arginine to Glutamine***

cGA → cAA

**DNA Position:** 821

SNP

GAGGCTGCC c(G or A)A CTGAAAGCT

Amino Acid Codon

**Rs Number:** rs3733890

**Location:** Chromosome 5q14.1

*** Frequency:**

| Population Category | GG | GA | AA |
|---|---|---|---|
| EUR | 48% | 41% | 11% |
| EAS | 52% | 41% | 7% |
| AFR | 55% | 41% | 4% |
| AMR | 32% | 52% | 16% |
| SAS | 52% | 43% | 5% |

## Betaine-homocysteine S-methyltransferase

Betaine-homocysteine methyltransferase (BHMT) is the enzyme responsible for remethylation of homocysteine via an alternate pathway using betaine as a methyl donor.[5] BHMT acts as a backup pathway to maintain SAM levels and is expressed primarily in the liver and kidney.[6]

### Health Implications

- The BHMT G742A polymorphism results in increased BHMT activity (also referred to as "upregulation"). Upregulation of BHMT may lead to lower levels of homocysteine as well as less dependency on folate and vitamin B-12 as methyl donors.
- Because this BHMT polymorphism results in increased activity, research suggests that this SNP is protective against many of the clinical conditions related to elevated homocysteine and folate deficiency.
- This G742A SNP has been associated with reduced all-cause mortality in breast cancer and decreased birth defect risk in some studies.[1-4]
- However, the overuse of choline as a substrate for methylation may have a negative metabolic consequence, because choline is needed for many other processes in the body.
  - For example, SNPs for this enzyme may result in decreased choline availability for the PEMT pathway, which is responsible for acetylcholine and phospholipid synthesis.[5]
- Abnormal choline metabolism may be associated with congenital abnormalities such as Down syndrome and neural tube defects.[7] These risks may be exacerbated by homozygous positive findings combined with low folate intake.

### Clinical Considerations

- Check choline and betaine levels; consider supplementation if applicable. Ensure adequate dietary choline intake.
- Assess likelihood of zinc insufficiency; evaluate plasma zinc and zinc/copper ratio.
- Assess SAM/SAH ratio and Methyl Balance Ratio to rule out excessive SAM production.

**References**
1. Boyles AL, et al. *Environ Health Perspect.* 2006;114(10):1547-1552.
2. Shaw GM, et al. *BMC Med Gen.* 2009;10:49.
3. Mostowska A, et al. *J Med Gen*. 2010;47(12):809-815.
4. da Costa KA, et al. *FASEB J.* 2014;28(7):2970-2978.
5. Obeid R. *Nutrients*. 2013;5(9):3481.
6. Sunden SL, et al. *Arch Biochem Biophys.* 1997;345(1):171-174.
7. Jaiswal SK, et al. *Eur J Clin Nutr.* 2017;71(1):45-50.

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## CBS C699T

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| T | T |
| Variant + | Variant + |

Potential Impact:

**Upregulation**

| Genotypes | Amino Acid |
|---|---|
| C C | Tyr Tyr |
| C T | Tyr Tyr |
| T T | Tyr Tyr |

**Amino Acid Position:** 233

***Tyrosine to Tyrosine***

TA**C** → TA**T**

**DNA Position:** 944

SNP

TGGCTCAC**TA(C** or **T)** GACACCACCG

Amino Acid Codon

**Rs Number:** rs234706

**Location:** Chromosome 21q22.3

## Cystathionine beta-synthase

Cystathionine beta-synthase (CBS) is the enzyme responsible for homocysteine's irreversible conversion to cystathionine. This is the first step in the transsulfuration pathway that ultimately leads to glutathione production.

### Health Implications

- The CBS enzyme is strongly regulated by the availability of SAM. Adequate SAM levels leads to an upregulation of the CBS enzyme, allowing homocysteine to be irreversibly committed to the transsulfuration pathway.[1]
- Most literature suggests that CBS C699T polymorphisms result in upregulation of CBS activity favoring transsulfuration and lowering homocysteine.[2,3]
- One study demonstrated the opposite effect in a Chinese population where CBS polymorphisms resulted in increased plasma homocysteine.[4] Therefore, debate exists regarding the impact of C699T polymorphism on enzyme activity.
- Despite the lack of agreement on enzyme activity, multiple studies demonstrate clinical associations with the C699T polymorphism. These include:
  - Reduced risk of lymphoma [5]
  - Reduced risk of venous disease [6,7]
  - Protective effects against deep vein thrombosis [6]
  - Decreased risk of coronary artery disease [8]

### Clinical Considerations

- Since this polymorphism is mostly considered to be protective, evaluate homocysteine levels in patients with "wild-type" (negative) CBS genotypes and address causes of elevated homocysteine.
- Some clinicians consider CBS polymorphisms to potentially "drain" methylation metabolites into the transsulfuration cycle. Evaluate overall methyl balance ratios and consider methylation support if warranted.
- Reduce levels of oxidative stress which further upregulate the CBS enzyme.
- Evaluate other transsulfuration metabolites (taurine, cystathionine, and glutathione) to determine if upregulation of CBS is likely. Assess met/sulf balance ratio.
- Ensure adequate supply of vitamin B-6 and iron, as these are cofactors for the CBS enzyme.

**References**


1. Stabler SP, et al. *Blood*. 1993;81(12):3404-3413.
2. DeStefano Vea. *Ann Hum Genet*. 1998;62(6):481-490.
3. Aras Ö, et al. *Clin Genet*. 2000;58(6):455-459.
4. Wu X, et al. *Hered Cancer Clin Pract*. 2014;12(1):2.
5. Li Q, et al. *Cancer Causes Control : CCC*. 2013;24(10):1875-1884.
6. Ayala C, et al. *Biomedica*. 2010;30(2):259-267.
7. Hendrix P, et al. *J Neurosurg*. 2017:1-7.
8. Kruger WD, et al. *Mol Genet Metab*. 2000;70(1):53-60.


*** Frequency:**

| Population Category | CC | C T | TT |
|---|---|---|---|
| EUR | 42% | 48% | 10% |
| EAS | 95% | 5% | <1% |
| AFR | 59% | 33% | 8% |
| AMR | 72% | 25% | 3% |
| SAS | 44% | 46% | 10% |

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## GNMT C1289T

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| C | T |
| Wild Type - | Variant + |

Potential Impact:
**Upregulation**

| Genotypes | Amino Acid |
|---|---|
| C C | Non-Coding |
| C T | Non-Coding |
| T T | Non-Coding |

**Amino Acid Position:** Untranslated Region

**DNA Position:** 4962

SNP
AGTGCTTATG (C or T) TTTAAGTGCG

**Rs Number:** rs10948059

**Location:** Chromosome 6p21.1

## Glycine N-methyltransferase

Glycine n-methyltransferase (GNMT) is an enzyme that plays a critical role in the disposal of excess s-adenosylmethionine (SAM), which is the body's main methyl donor. GNMT removes methyl groups from SAM by conjugating them with glycine to form the byproduct sarcosine.

### Health Implications

- GNMT acts as a SAM/SAH buffer by disposing excess SAM through conjugation with glycine. This process is downregulated in response to low 5-MTHF and SAM levels. Increased GNMT activity could potentially lead to increased sarcosine levels, which has been associated with prostate cancer risk in several studies.[1-3]
  - However, in one study of Taiwanese men (where GNMT polymorphism is less common), GNMT polymorphism showed a protective effect on prostate cancer risk, which highlights the differences in SNP frequencies in different populations.[4]
- The C1289T polymorphism results in upregulation of the GNMT enzyme which increases the rate of SAM disposal and sarcosine creation. This may limit SAM availability for methylation reactions and reduce its regulatory effects on the transsulfuration and/or folate pathways.
- GNMT is also involved in detoxification and antioxidant pathways. This may play a role in the increased cancer risk demonstrated in homozygous negative individuals and in animal models.
- GNMT SNPs have been shown to play a role in elevating plasma homocysteine, particularly with folate-restriction.[5]

### Clinical Considerations

- Evaluate methylation balance, SAM/SAH, and sarcosine levels.
- Ensure adequate levels of glycine, as this is a substrate for the reaction catalyzed by GNMT and is also involved in glutathione synthesis.

### * Frequency:

| Population Category | CC | CT | TT |
|---|---|---|---|
| EUR | 29% | 47% | 24% |
| EAS | 70% | 28% | 2% |
| AFR | 23% | 43% | 34% |
| AMR | 50% | 44% | 6% |
| SAS | 36% | 47% | 17% |

**References**
1. Lucarelli G, et al. *Prostate*. 2012;72(15):1611-1621.
2. Jentzmik F, et al. *Eur Urol*. 2010;58(1):12-18.
3. Sreekumar A, et al. *Nature*. 2009;457(7231):910.
4. Chen M, et al. *PloS one*. 2014;9(5):e94683.
5. Beagle B, et al. *J Nutr*. 2005;135(12):2780-2785.

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## MAT1A D18777A

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| G | A |
| Wild Type - | Variant + |

Potential Impact:
**Downregulation**

| Genotypes | Amino Acid |
|---|---|
| G G | Non-Coding |
| G A | Non-Coding |
| A A | Non-Coding |

**Amino Acid Position:** Untranslated Region

**DNA Position:** 23777

SNP
GCTTTTCTCT(G or A)TAATGTGTCA

**Rs Number:** rs3851059

**Location:** Chromosome 10q22.3

## Methionine adenosyltransferase

Methionine adenosyltransferase (MAT) is the enzyme that catalyzes the conversion of methionine into the body's main methyl donor, s-adenosylmethionine (SAM). This enzyme requires magnesium as a cofactor and is downregulated by oxidative stress, such as alcohol and free radical damage.

### Health Implications

- Methionine adenosyltransferase (MAT) activity is critical to methylation. There are a few MAT1A genetic polymorphisms studied that lead to MAT1A deficiency (also known as Mudd's Disease), but this condition is extremely rare.
- The D18777A SNP is fairly common in the human population and has associations with cardiovascular disease risk.[1]
- Although literature is scant on this mutation, some studies have demonstrated higher homocysteine levels with this polymorphism.[2] Another study also demonstrated that this correlation was modulated by overall dietary fat intake.[3]
- Another study demonstrated that the D18777A SNP was associated with higher rates of stroke independent of homocysteine levels, which was hypothesized to be due to methylation activity impairment.[1]

### Clinical Considerations

- Evaluate methylation balance, SAM/SAH, and sarcosine levels.
- Reduce levels of oxidative stress, such as free radical exposure and alcohol intake as these can further impair the MAT1A enzyme.
- Ensure adequate levels of MAT1A cofactors such as magnesium and potassium. Consider testing RBC magnesium and potassium.
- Patients with this polymorphism may have higher homocysteine in response to dietary fat intake than those without.[3] Monitor advanced cardiovascular risk markers if clinically appropriate.

### * Frequency:

| Population Category | GG | G A | AA |
|---|---|---|---|
| EUR | 50% | 43% | 7% |
| EAS | 36% | 48% | 16% |
| AFR | 62% | 34% | 4% |
| AMR | 52% | 40% | 8% |
| SAS | 42% | 45% | 13% |

**References**
1. Lai CQ, et al. *Am J Clin Nutr*. 2010;91(5):1377-1386.
2. Beagle B, et al. *J Nutr*. 2005;135(12):2780-2785.
3. Huang T, et al. *Nutr Metab Cardiovasc Dis*. 2012;22(4):362-368.

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## MTR A2756G

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| A | A |
| Wild Type - | Wild Type - |

Potential Impact:
**No Upregulation**

| Genotypes | Amino Acid |
|---|---|
| A A | Asp Asp |
| A G | Asp Gly |
| G G | Gly Gly |

**Amino Acid Position:** 919

***Aspartate to Glycine***

G A C → G G C

**DNA Position:** 3179

SNP

ATTAGACAG G(A or G)C CATTATGAG

Amino Acid Codon

**Rs Number:** rs1805087

**Location:** Chromosome 1q43

## Methionine synthase

Methionine synthase (MS/MTR) is responsible for converting homocysteine back into methionine by using 5-MTHF as a methyl donor. This reaction requires zinc and active B-12 (methylcobalamin) as cofactors and is the main pathway responsible for homocysteine recycling in every cell.

### Health Implications

- The A2756G polymorphism is the most common MTR SNP discussed in the literature.
- It is generally accepted that this SNP upregulates the MTR enzyme leading to lower homocysteine levels.[1]
- The impact of this SNP on global DNA methylation is debated in the literature, however clinical associations with the A2756G polymorphism include congenital birth defects such as spina bifida, cleft lip/palate, and cardiac defects.[2–4]
- One hypothesis is that as the MTR enzyme is at the junction between the folate pathway and the methylation pathway, upregulation of MTR may shunt folate groups to the methylation cycle at the expense of other folate needs, such as purine/nucleotide synthesis.
- Several epidemiological studies on MTR polymorphism have demonstrated risk associations with various cancers, evidence remains controversial.[5–7] Many of these risk associations appear to be population/ethnicity specific, which could be due to gene-gene interactions with MTRR and MTHFR.

### Clinical Considerations

- Compare any MTR polymorphisms with MTHFR and MTRR genetic results.
- Evaluate homocysteine, SAM/SAH ratio, and monitor biomarkers for vitamin B-12 and folate.
- Ensure adequate dietary intake of folate and vitamin B-12.

### * Frequency:

| Population Category | AA | A G | GG |
|---|---|---|---|
| EUR | 69% | 30% | 1% |
| EAS | 72% | 25% | 3% |
| AFR | 47% | 42% | 11% |
| AMR | 65% | 33% | 2% |
| SAS | 42% | 47% | 11% |

**References**
1. Ho V, et al. *Genes Nutr*. 2013;8(6):571-580.
2. Wang W, et al. *Genet Test Mol Biomarkers*. 2016;20(6):297-303.
3. Klerk M, et al. *Thromb Res*. 2003;110(2-3):87-91.
4. Doolin MT, et al. *Am J Hum Genet*. 2002;71(5):1222-1226.
5. Bleich S, et al. *Epigenomics*. 2014;6(6):585-591.
6. Hosseini M. *Pol J of Pathol*. 2013;64(3):191-195.
7. Jiang-hua Q, et al. *Tumour Biol*. 2014;35(12):11895-11901.

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## MTRR A66G

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| G | G |
| Variant + | Variant + |

Potential Impact:

**Downregulation**

| Genotypes | Amino Acid |
|---|---|
| A A | Ile Ile |
| A G | Ile Met |
| G G | Met Met |

**Amino Acid Position:** 22

***Isoleucine to Methionine***

AT A → AT G

**DNA Position:** 203

SNP

CAGAAGAA **AT(A** or **G)** TGTGAGCAAG

Amino Acid Codon

**Rs Number:** rs1801394

**Location:** Chromosome 5p15.31

## * Frequency:

| Population Category | AA | A G | GG |
|---|---|---|---|
| **EUR** | 38% | 34% | 28% |
| **EAS** | 54% | 37% | 9% |
| **AFR** | 59% | 36% | 5% |
| **AMR** | 26% | 57% | 17% |
| **SAS** | N/A | N/A | N/A |

## Methionine synthase reductase

Methionine synthase reductase (MTRR) is an enzyme that works in cooperation with methionine synthase (MTR) by reducing oxidized forms of vitamin B-12 to be reused. This allows MTR to continue to convert homocysteine back into methionine.

### Health Implications

- MTRR polymorphisms result in decreased enzyme activity and therefore a decreased capacity to recycle oxidized cobalamin (vitamin B-12). This decreased enzyme activity can affect methylation capacity by limiting the amount of active B-12 available for homocysteine conversion.[1]
- Both MTRR polymorphisms can result in homocysteine elevation, independent of folate, B-12, or B-6 levels.[2]
- The A66G polymorphism is the most commonly studied MTRR SNP. It has been associated with numerous clinical conditions, such as various cancers, birth defects, metabolic syndrome, mood disorder, and elevated homocysteine.[3–5]
- The A66G polymorphism has also been shown to correlate with global DNA hypomethylation, which is a direct marker for methylation impairment.

### Clinical Considerations

- Compare any MTRR polymorphisms with MTHFR and MTR genetic results Evaluate homocysteine, SAM/SAH ratio, and monitor biomarkers for vitamin B-12 and folate.
- Ensure adequate dietary intake of folate and vitamin B-12, consider repletion with methylcobalamin in these individuals.
- Ensure adequate vitamin B-2 and B-3 status, as they are cofactors for the MTRR enzyme.
- Assess antioxidant capacity, as oxidative stress impacts levels of methylcobalamin.

**References**
1. Olteanu H, et al. *Biochemistry.* 2002;41(45):13378-13385.
2. Gaughan DJ, et al. *Atherosclerosis.* 2001;157(2):451-456.
3. Jamerson BD, et al. *Int J Geriatr Psychiatry.* 2013;28(9):925-932.
4. Hassan FM, et al. *Gene.* 2017;629:59-63.
5. Guo QN, et al. *BioMed Res Int.* 2017;2017:3043476.

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## SHMT1 C1240T

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| C | T |

Wild Type - Variant +

Potential Impact:

**Downregulation**

| Genotypes | Amino Acid |
|---|---|
| C C | Leu Leu |
| C T | Leu Phe |
| T T | Phe Phe |

**Amino Acid Position:** 474

***Leucine to Phenylalanine***

CTC → TTC

**DNA Position:** 1631

SNP

CTTCGCCTCT (C or T) TC TTCCCTCT

Amino Acid Codon

**Rs Number:** rs1979277

**Location:** Chromosome 17p11.2

*** Frequency:**

| Population Category | CC | C T | TT |
|---|---|---|---|
| **EUR** | 45% | 43% | 12% |
| **EAS** | 87% | 13% | <1% |
| **AFR** | 33% | 47% | 20% |
| **AMR** | 59% | 41% | <1% |
| **SAS** | N/A | N/A | N/A |

## Serine hydroxymethyltransferase 1

Serine hydroxymethyltransferase 1 (SHMT) is responsible for maintaining a relative balance of folate groups between the methylation cycle and the folate cycle. It uses serine and glycine to exchange methyl groups between THF and 5,10-MTHF as needed.

### Health Implications

- SHMT1 is a bidirectional enzyme that can create a short-cut for methylation of homocysteine back to methionine through rapid creation of 5-MTHF. However, SHMT generally gives metabolic priority to nucleotide synthesis over SAM synthesis.[1]
- The C1240T polymorphism alters the SHMT1 enzyme function to favor the folate cycle over the methylation cycle to an even greater extent. Ultimately, this imbalance can cause reduced circulating folate (5-MTHF) levels and increased homocysteine.[2]
- This SNP adversely affects DNA synthesis, methylation systems, and causes genome instability. It eventually leads to oncogene overexpression and tumor suppressor gene inactivation.[1,3]
- The C1240T SNP has been associated with several clinical conditions, including various cancers and exacerbation of cardiovascular disease risk associated with MTHFR.[4-6]

### Clinical Considerations

- Evaluate MTHFR SNP which may exacerbate CVD risk and low folate status.
- Consider supplementation with 5-MTHF and other methyl donors if high homocysteine or low SAM/SAH ratio.
- Consider additional B-vitamin supplementation to support MTHFR enzyme, such as vitamins B-2, B-3, and B-12.

**References**
1. Choi S-W, Mason JB. *J Nutr.* 2000;130(2):129-132.
2. Lightfoot TJ, et al. *Cancer Epidemiol Biomarkers Prev.* 2005;14(12):2999-3003.
3. Zijno A, et al. *Carcinogenesis.* 2003;24(6):1097-1103.
4. Wang Y-W, et al. *Chin J Cancer.* 2015;34(12):573-582.
5. Carmona B, et al. *Am J Clin Nutr.* 2008;88(5):1413-1418.
6. Wernimont SM, et al. *J Nutr.* 2011;141(2):255-260.

*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## MTHFR C677T

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| C | T |

Wild Type - Variant +

Potential Impact:

**Downregulation**

| Genotypes | Amino Acid |
|---|---|
| C C | Ala Ala |
| C T | Ala Val |
| T T | Val Val |

**Amino Acid Position:** 222

***Alanine to Valine***

G C C → G T C

**DNA Position:** 894

SNP

TCTGCGGGA G(C or T) C GATTTCATC

Amino Acid Codon

**Rs Number:** rs1801133

**Location:** Chromosome 1p36.22

*** Frequency:**

| Population Category | CC | C T | TT |
|---|---|---|---|
| EUR | 47% | 44% | 9% |
| EAS | 37% | 47% | 16% |
| AFR | 81% | 19% | <1% |
| AMR | 32% | 52% | 16% |
| SAS | 68% | 30% | 2% |

## 5,10-methylenetetrahydrofolate reductase

Methylenetetrahydrofolate reductase (MTHFR) is a key regulatory enzyme which converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (5-MTHF). This step activates folate to be used for homocysteine (Hcy) conversion to methionine, instead of nucleotide synthesis.

### Health Implications

- The C677T polymorphism downregulates enzymatic activity, which can limit methylation reactions in the body. The C677T polymorphism results in an increased risk of high homocysteine and an increased tendency for lower folate levels.[1,2]
- Homozygosity for 677 (+/+) results in 60-70% reduction in MTHFR enzyme activity. Heterozygosity for 677 (-/+) results in 30-40% reduction in MTHFR enzyme activity.[3]
- Lower levels of B-vitamin and folate increase the risk of elevated homocysteine related to MTHFR SNPs.[2]
- Homozygous C677T subjects have higher Hcy levels, while heterozygous subjects have mildly raised Hcy levels compared to controls.[4]
- MTHFR C677T SNPs have been associated with many disease processes including:
  - Cardiovascular disease [5-7]
  - Depression and schizophrenia [8,9]
  - Increased risk of birth defects and Down's syndrome [10]
  - Psoriasis
  - Diabetes
  - Parkinson's disease
  - Various cancers [4]

### Clinical Considerations

- Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods.
- Evaluate homocysteine, SAM, and SAH levels.
- Supplementation with methylated folate and folate-rich foods may help lower Hcy and mitigate risk.[11]
- Evaluate the status of vitamin B-2 and B-3 (MTHFR enzyme cofactors).

**References**


1. Yang Q, et al. *Am J Clin Nutr*. 2012;95(5):1245-1253.
2. Garcia-Minguillan CJ, et al. *Genes Nutr*. 2014;9(6):435.
3. Weisberg IS, et al. *Atherosclerosis*. 2001;156(2):409-415.
4. Liew S-C, et al. *Eur J Med Genet*. 2015;58(1):1-10.
5. Zhang P, et al. *Angiology*. 2015;66(5):422-432.
6. Yang KM, et al. *Biomed Rep*. 2014;2(5):699-708.
7. Cui T. *Int J Neurosci*. 2015.
8. Wu YL, et al. *Prog Neuropsychopharmacol Biol Psychiatry*. 2013;46:78-85.
9. Hu CY, et al. *J Neural Transm (Vienna)*. 2015;122(2):307-320.
10. Yadav U, et al. *Metab Brain Dis*. 2015;30(1):7-24.
11. Zhao M, et al. *Stroke*. 2017;48(5):1183-1190.


*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## MTHFR A1298C

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| A | A |
| Wild Type - | Wild Type - |

Potential Impact:

**No Downregulation**

| Genotypes | Amino Acid |
|---|---|
| A A | Glu Glu |
| A C | Glu Ala |
| C C | Ala Ala |

**Amino Acid Position:** 429

***Glutamate to Alanine***

G A A → G C A

**DNA Position:** 1515

SNP

ACCAGTGAA G(A or C)A AGTGTCTTT

Amino Acid Codon

**Rs Number:** rs1801131

**Location:** Chromosome 1p36.22

## 5,10-methylenetetrahydrofolate reductase

Methylenetetrahydrofolate reductase (MTHFR) is a key regulatory enzyme which converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate (5-MTHF). This step activates folate to be used for homocysteine conversion to methionine, instead of nucleotide synthesis.

### Health Implications

- The A1298C homozygous SNP mutation downregulates enzyme activity but may not independently affect folate or homocysteine levels.[1] However, a combined heterozygosity for both 677T and 1298C mutations does result in significant plasma homocysteine elevation.[1,2]
- Heterozygosity for only 1298 (-/+) has not been shown to affect overall MTHFR enzyme activity, however, homozygosity for 1298 (+/+) results in 30-40% reduction in MTHFR enzyme activity.[3]
- MTHFR A1298C SNPs have been associated with many disease processes including:
  - Cardiovascular disease [4-6]
  - Male infertility [7,8]
  - Increased risk of birth defects [9]
  - Certain cancer types[10-12]

### Clinical Considerations

- Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods.
- Evaluate homocysteine, SAM, and SAH levels.
- Supplementation with methylated folate and folate-rich foods may help lower Hcy and mitigate risk.[13]
- Evaluate the status of vitamin B-2 and B-3 (MTHFR enzyme cofactors).

### * Frequency:

| Population Category | AA | A C | CC |
|---|---|---|---|
| EUR | 43% | 45% | 12% |
| EAS | 63% | 33% | 4% |
| AFR | 78% | 21% | 1% |
| AMR | 62% | 34% | 4% |
| SAS | 39% | 44% | 17% |


**References**

1. Isotalo PA, et al. *Am J Hum Genet*. 2000;67(4):986-990.
2. van der Put NM, et al. *Am J Hum Genet*. 1998;62(5):1044-1051.
3. Weisberg IS, et al. *Atherosclerosis*. 2001;156(2):409-415.
4. Kang S, et al. *J Clin Neurosci*. 2014;21(2):198-202.
5. Lv Q, et al. *Genet Mol Res*. 2013;12(4):6882-6894.
6. Zhang MJ, et al. *Cerebrovasc Dis*. 2014;38(6):425-432.
7. Eloualid A, et al. *PloS one*. 2012;7(3):e34111.
8. Shen O, et al. *Ann Hum Genet*. 2012;76(1):25-32.
9. Xuan C, et al. *Sci Rep*. 2014;4:7311.
10. Qi X, et al. *Tumour Biol*. 2014;35(3):1757-1762.
11. Qi YH, et al. *Clin Res Hepatol Gastroenterol*. 2014;38(2):172-180.
12. Qin X, et al. *PloS one*. 2013;8(2):e56070.
13. Zhao M, et al. *Stroke*. 2017;48(5):1183-1190.


*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK

**3542 Methylation Genomics** - Buccal Swab
*Methodology: PCR Sequencing*

## COMT V158M

Your Genotype:

| Allele 1 | Allele 2 |
|---|---|
| G | A |
| Wild Type - | Variant + |

Potential Impact:
**Downregulation**

| Genotypes | Amino Acid |
|---|---|
| G G | Val Val |
| G A | Val Met |
| A A | Met Met |

**Amino Acid Position:** 158

***Valine to Methionine***

GTG →ATG

**DNA Position:** 721

SNP

TTTCGCTGGC (G or A)TGAAGGACAA

Amino Acid Codon

**Rs Number:** rs4680

**Location:** Chromosome 38.p12

## Catechol-O-methyltransferase

Catechol-O-Methyltransferase (COMT) is a key enzyme involved in the deactivation of catechol compounds, including catecholamines, catechol estrogens, catechol drugs such as L-DOPA, and various chemicals and toxins such as aryl hydrocarbons.

### Health Implications

- COMT polymorphisms result in decreased enzyme activity. Individuals with COMT SNPs may have an increased risk of inefficient methylation of catecholamines, estrogens, and toxins.[1,2]
- The most common genotype of COMT in most populations is heterozygous (+/-). Individuals with a homozygous positive (+/+) genotype for COMT have a 3-4-fold reduction in COMT activity.
- COMT polymorphisms have been implicated in mood disturbances such as anxiety, panic disorder, eating disorder, aggressiveness, anger, alcoholism, and severity of bipolar disorder.[3–5]
- COMT polymorphism has been implicated in risk of breast cancer, particularly in women with prolonged estrogen exposure;[6,7] or in women with low folate and high homocysteine.[8] Also, COMT SNPs have been shown to correlate with higher estrogen levels with estrogen replacement therapy.[9]
- Fibromyalgia and migraine have been associated with COMT polymorphisms as well.[10,11]

### Clinical Considerations

- Evaluate methylation pathway to locate any potential backup.
- Ensure adequate B6, B12, folate, magnesium, betaine, and methionine to ensure adequate SAM production.
- SAM-e supplementation may be considered, as it is the cofactor for COMT, however, this therapy is contraindicated in bipolar disorder.
- Minimize stress, since catecholamine levels may already be high.
- Make sure to appropriately monitor estrogen levels and estrogen metabolites, especially if your patient is on estrogen replacement therapy.
- Consider additional antioxidant support, especially if low levels of glutathione are reported.

### * Frequency:

| Population Category | GG | GA | AA |
|---|---|---|---|
| EUR | 22% | 53% | 25% |
| EAS | 43% | 47% | 10% |
| AFR | 46% | 45% | 9% |
| AMR | 54% | 37% | 8% |
| SAS | 37% | 41% | 22% |


**References**

1. Lachman et al. *Pharmacogenetics*. 1996;6(3):243-250.
2. Mannisto et al. *Pharmacol Rev*. 1999;51(4):593-628.
3. Woo JM, et al. *Am J Psychol*. 2002;159(10):1785-1787.
4. Rujescu D, et al. *Biol Psychiatry*. 2003;54(1):34-39.
5. Papolos DF, et al. *Mol Psychiatry*. 1998;3(4):346-349.
6. Huang CS, et al. *Cancer Res*. 1999;59(19):4870-4875.
7. Lavigne JA, et al. *Cancer Res*. 1997;57(24):5493-5497.
8. Goodman JE, et al. *Carcinogenesis*. 2001;22(10):1661-1665.
9. Worda C, et al. *Hum Reprod*. 2003;18(2):262-266.
10. Gursoy S, et al. *RheumatolInt*. 2003;23(3):104-107.
11. Emin Erdal M, et al. *Brain Res Mol Brain Res*. 2001;94(1-2):193-196.


*Population frequency data is from 1000 GENOMES project as sourced from NCBI dbSNP. The population categories are listed below:
**EUR (European):** Americans with Northern and Western European Ancestry, Toscani, Finnish, British, Spanish
**EAS (East Asian):** Han Chinese (Beijing), Japanese (Tokyo), Southern Han Chinese, Chinese Dai, Kinh (Vietnam)
**AFR (African):** Nigerian, Kenyan, Gambian, Mendi (Sierra Leone), African American, African Caribbean
**AMR (Ad Mixed American):** Mexican, Puerto Rican, Colombian, Peruvian
**SAS (South Asian):** Americans of Gujarati descent (India), Punjabi (Pakistan), Bengali (Bangladesh), Sri Lankan/Indian in UK