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## **Functional Imbalance Scores**

: Moderate Need for Support

**Need for Antioxidant Support Oxidative Stress** 

Key



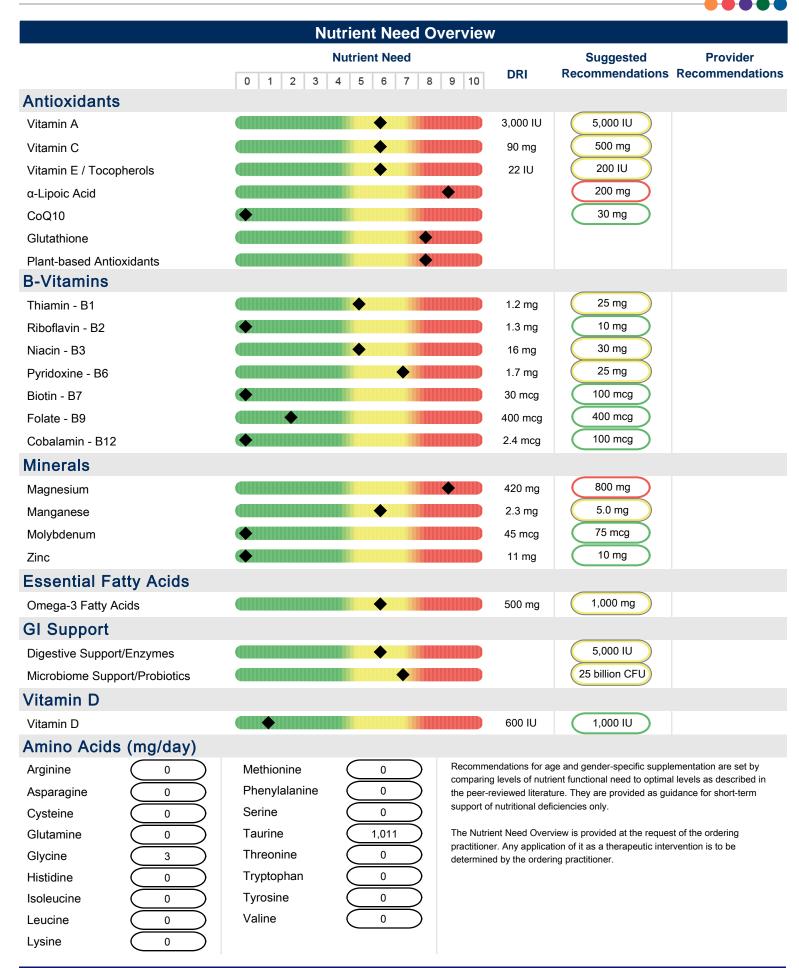
Cystine Cysteine Lipid Peroxides 8-OHdG Glutathione Taurine Citric Acid cis-Aconitic Acid

: Minimal Need for Support Need for Mitochondrial Support Mitochondrial Dysfunction Glutathione CoQ10 Magnesium **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 Manganese

**Need for** Inflammation Support Omega Imbalance 6  $\nabla$ Omega-3 Index Omega 6/3 Ratio α-Linolenic Acid Arachidonic Acid Linoleic Acid y-Linolenic Acid Dihomo-y-linolenic Acid

Need for **Reduced Exposure Toxic Exposure** Lead Mercury α-Hydroxyisobutyric Acid Δ α-Ketophenylacetic Acid Arsenic Cadmium Pyroglutamic Acid Orotic Acid Citric Acid cis-Aconitic Acid Isocitric Acid Glutaric Acid

(8-10): High Need for Support Need for **Methylation Support** Methylation Imbalance Methylmalonic Acid Methionine Glutathione **FIGLU** Sarcosine Vanilmandelic Acid Arginine Glycine Serine Creatinine



#### **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 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.

#### 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
- 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.

### **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.).

#### 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.

#### 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  $\alpha$ -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.

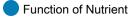
#### Glutathione

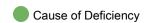




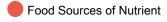
- Glutathione (GSH) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection, inflammation and
- 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.

## **KFY**









#### **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
- 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.

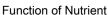
#### Cobalamin - B12

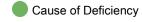




- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA,
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 blockers, PPIs), vegan diets, diabetic meds, cholestyramine, chloramphenicol, neomycin or
- 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.







Complications of Deficiency



#### **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.

#### 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).

#### 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.

#### 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**

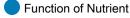
#### Need for Omega-3s

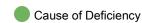


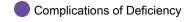


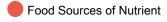
- Omega-3 (O3) and Omega-6 (O6) fatty acids are polyunsaturated fatty acids that cannot be synthesized by the human body. They are classified as essential nutrients and must be obtained from dietary sources.
- The standard American diet is much higher in O6 than O3 fatty acids. Deficiency of EFAs may 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**









## 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**



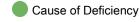


- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal 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** 



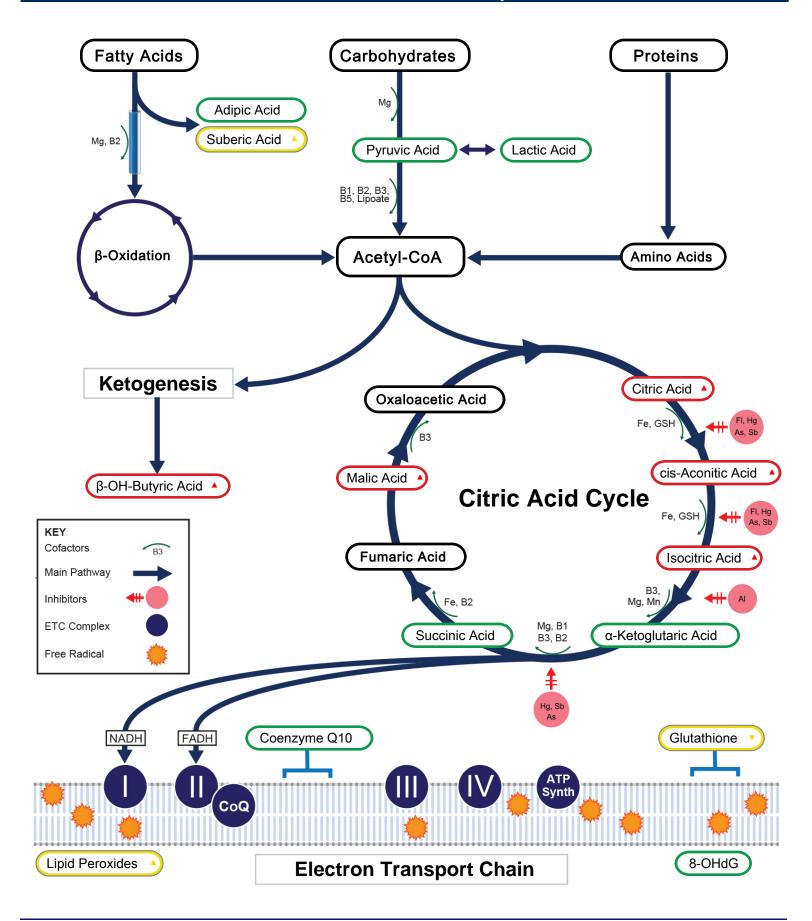


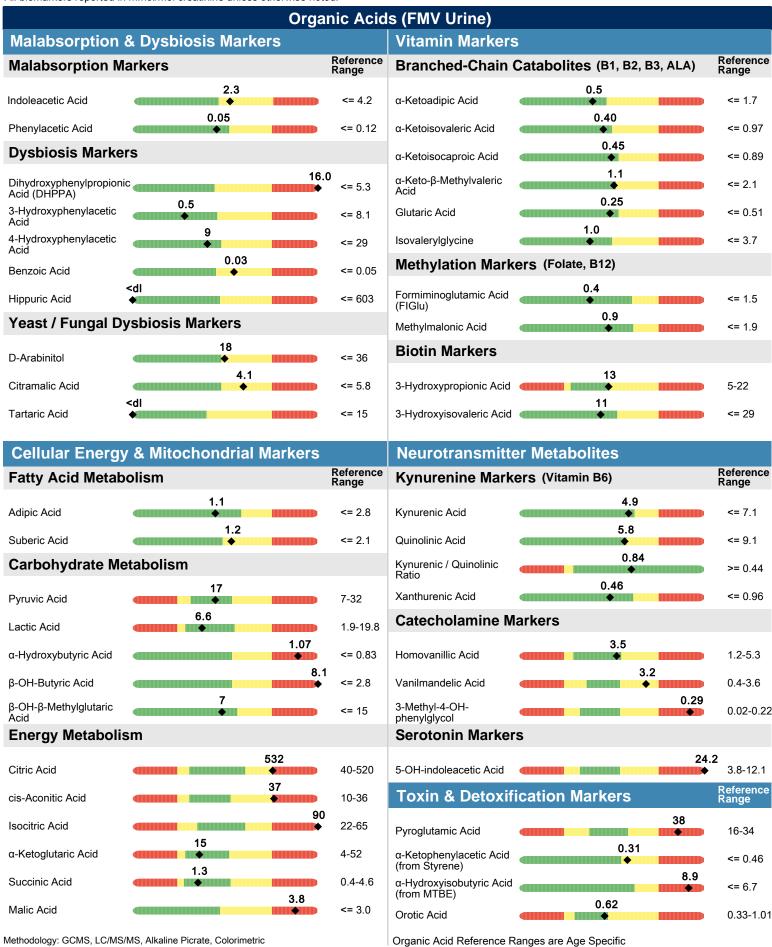
Complications of Deficiency



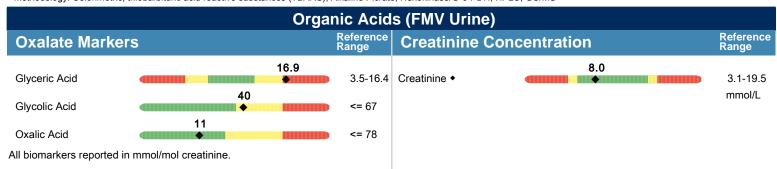
Food Sources of Nutrient

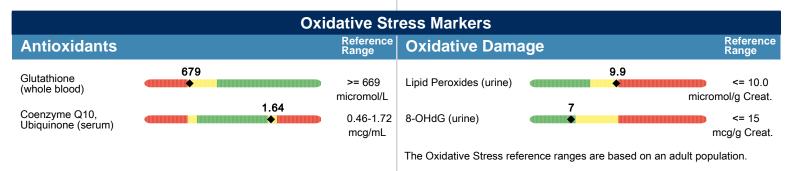
## **Oxidative Stress & Mitochondrial Dysfunction**



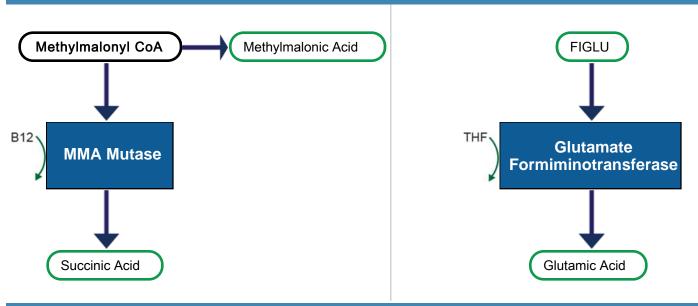




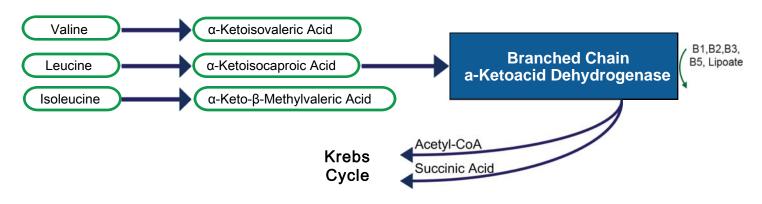




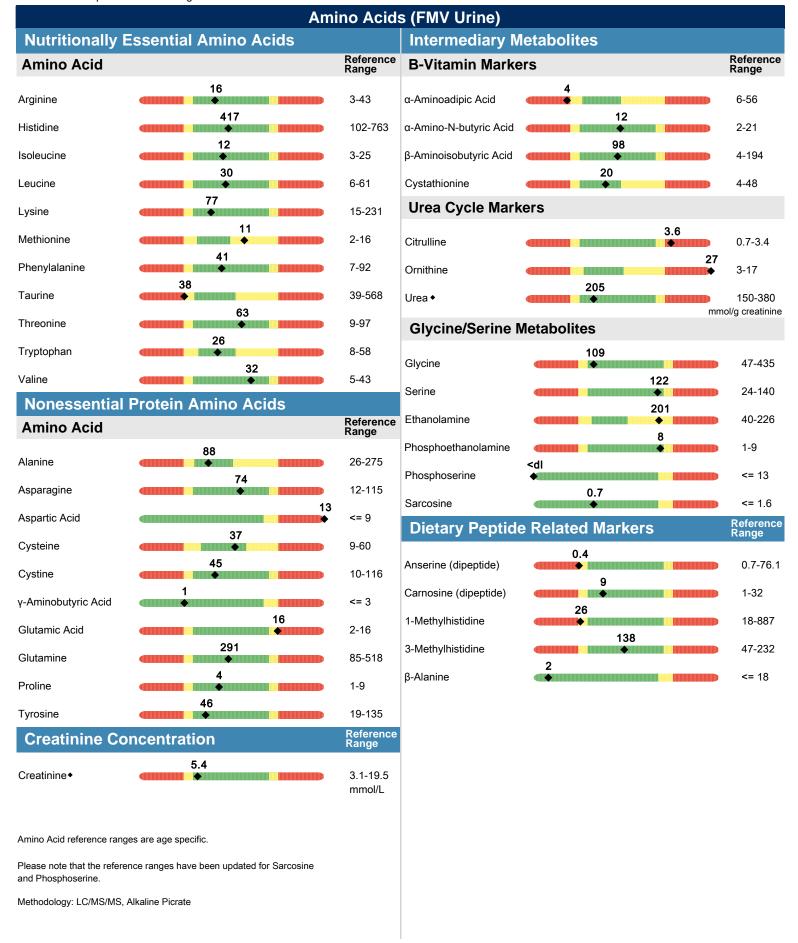
# Pathways Methylation Markers



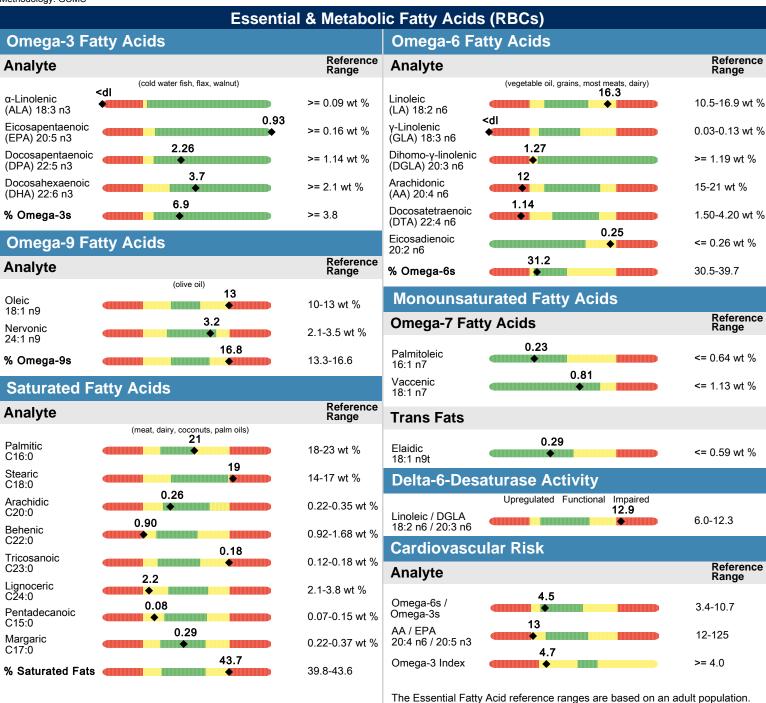
## **Branch-Chain Amino Acid Metabolism**





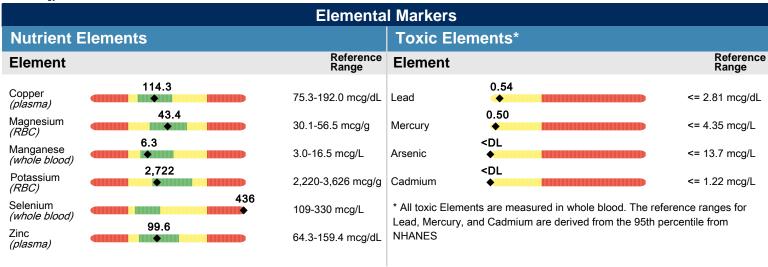






## **Fatty Acid Metabolism** Omega-3 Metabolism Omega-6 Metabolism **Enzyme** α-Linolenic Acid Linoleic Acid **Delta-6-Desaturase** Important Regulators: B2, B3, B6, Vitamin C, Insulin, Zn, Mg Stearidonic Acid y-Linolenic Acid **Elongase** Important Regulators: B3, B5, B6, Biotin, Vitamin C Eicosatetraenoic Acid Dihomo-y-Linolenic Acid **Anti-Inflammatory** Series 1 Prostaglandins **Delta-5-Desaturase** Important Regulators: B2, B3, B6, Vitamin C, Insulin, Zn, Mg Eicosapentaenoic Acid Arachidonic Acid **Pro-Inflammatory Anti-Inflammatory Eicosanoids Eicosanoids Elongase** Important Regulators: B3, B5, B6, Biotin, Vitamin C Docosapentaenoic Acid Docosatetraenoic Acid **Elongase** Delta-6-Desaturase Docosahexaenoic Acid

Methodology: ICP-MS



The Elemental reference ranges are based on an adult population.

## **Commentary**

For more information regarding NutrEval clinical interpretation, please refer to the NutrEval Support Guide at <a href="https://www.gdx.net/nutrevalguide">www.gdx.net/nutrevalguide</a>.

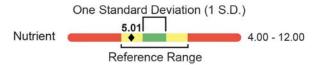
Vitamin D (Serum)							
Methodology: Chemiluminescent		Result	Reference Range				
25 - Hydroxyvitamin D ◆		81	30-100 ng/mL	There is no consensus in the literature regarding optimal levels			
Deficiency: Insufficiency: Sufficient: Recommended: Excessive:	<20 ng/mL 20-29 ng/mL 30-100 ng/mL 50-80 ng/mL >100 ng/mL			of 25-Hydroxyvitamin D. Higher levels of 25-Hydroxyvitamin D may be concerning in patients with renal failure. Levels below 30 ng/mL are considered insufficient by most medical associations			
•	J Clin Endocrinol M	<i>letab</i> .2011;96(7):1911-1930 nindcouncil.org/	).				

Homocysteine (Plasma)							
Methodology: Chemiluminescent	Result	Reference Range		The reference range for			
Homocysteine	5.6	5.2-11.4	micromol/L	The reference range for homocysteine is based on the sex-specific 5th to 95th percentile values for men and women (20 to 39 years of age) in the NHANES nutritionally replete cohort. Annals of Internal Medicince 1999; 131 (331-338).			

## **Lab Comments**

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

The **Reference Range** is a statistical interval representing 95% or 2 Standard Deviations (2 S.D.) of the reference range population. One Standard Deviation (1 S.D.) is a statistical interval representing ~68% of the reference population. Values between 1 and 2 S.D. are not necessarily abnormal. Clinical Correlation is suggested.





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## $\overline{Apo} E$

## Location:

### Chromosome 19 APOE

APO E2: cys / cys APO E3: cys / arg APO E4: arg / arg Your Genotype:

The two SNPs lead to 3 possible variants for each chromosome, known as ApoE2, E3, & E4.

## Apolipoprotein E: CHOLESTEROL REGULATION

Apolipoprotein E (Apo E) plays a key role in lipid metabolism by helping to remove dietary cholesterol (chylomicrons and VLDL) from the bloodstream.

#### **Health Implications**

- · The E3/E3 genotype is the most common (accounting for >50% of most populations) and is the genotype against which E2 and E4 are compared.
- · E3/E3 may be protective against stroke compared with other genotypes, particularly in females.
- · ApoE3 confers only a moderate tendency toward elevated total- and LDL cholesterol, and lower HDL-C.
- · Risk is intermediate between E2 and E4 for atherosclerosis, MI, stroke (in smokers), and osteoporosis.
- · The E3 genotype led to an approximate 90% increase in the levels of TG in the presence of abdominal obesity.

#### **Clinical Management Considerations**

- · Effects of cholesterol and dietary fat on serum cholesterol levels are least profound with the E2 allele and greatest with the E4 allele; thus, dietary fat restriction produces a moderate cholesterol response in E3/E3 individuals.
- · Carbohydrate intake may be inversely correlated with HDL-C.
- · Alcohol may have a neutral effect on LDL-C.
- · Avoid smoking, which increases risk of CAD in this genotype.
- · Lipid response to statins, and triglyceride response to fibrates, are usually the best in E2 > E3 > E4; studies are mixed.
- · HT generally improves the lipid profile in all genotypes, including post-menopausal E3 carriers.

Kev

Neither chromosome carries the genetic variation.

One chromosome (of two) carries the genetic variation.

+ Both chromosomes carry the genetic variation. (You inherit one chromosome from each parent)

Gene activity increased

Gene activity decreased



MTHFR	5,10-methyltetrahydrofolate reductase : METHYLATION
Location:	5,10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, facilitating the formation of methyltetrahydrofolate, a required cofactor in the remethylation of homocysteine (Hcy) to methionine.
Chromosome 1 C677T Your Genotype:	Health Implications  · Baseline "normal" MTHFR enzyme activity, suggesting adequate formation of methyl-THF  · An elevated homocysteine level is still possible with normal MTHFR capacity in the presence of B-vitamin
	deficiency
A1298C Your Genotype:	Clinical Management Considerations  · Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods

## COMTCatechol-O-MethylTransferase: METHYLATION 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 catechol metabolites of Location: various chemicals and toxins, such as aryl hydrocarbons. Chromosome 22.11q V158M **Health Implications** Your Genotype: · Normal COMT enzyme activity, resulting in efficient methylation of catecholamines and estrogens · Less sensitivity to stress, compared to the other genotypes, due to lower baseline catecholamine levels · Lower baseline brain dopamine is associated with lower cognitive stability (e.g., focus) but greater cognitive flexibility (e.g., ability to adapt to external changes) compared to the other genotypes Superior cognitive function possible in Parkinson's disease patients; however, dopaminergic agents may compromise cognition · Preliminary findings suggest possible decreased risk of cardiovascular events, which might be abolished by taking aspirin · Possible increased risk of schizophrenia (conflicting studies), symptomology, and inferior cognitive performance in schizophrenics **Clinical Management Considerations** · Ensure adequate B6, B12, folate, magnesium, and methionine for general methylation support · Cognitive efficiency may be improved by stimulation · Possibly best methylphenidate (Ritalin®) response in children with ADHD (mixed studies)

# TNF-α Tumor Necrosis Factor-alpha: INFLAMMATION TNF-alpha (TNF- $\alpha$ ) is a pro-inflammatory cytokine secreted that is secreted from activated macrophages. TNF- $\alpha$ plays an important role in host defense against infection; however, excessive release of the cytokine increases Location: inflammation and oxidative stress. Chromosome 6 **Health Implications** -308G-A · Decreased production of TNF-α, decreased inflammatory tendency and oxidative stress compared to the other Your Genotype: genotypes · Reduced risk of various autoimmune diseases or their severity; less risk of insulin resistance, obesity, and some cancers (including non-Hodgkin's lymphoma, cervical CA, liver CA, and oral squamous cell CA) Reduced risk of asthma or irritant contact dermatitis; less chance of developing sepsis following severe trauma · Possible increased risks of ischemic stroke in adults (esp. Asians), depression or bipolar disorder, and multiple sclerosis (studies are mixed) **Clinical Management Considerations** · No particular treatment indicated; maintain a healthy lifestyle to minimize inflammation. · Generally positive therapeutic response to anti-TNF- $\alpha$ medications (e.g., etanercept) in rheumatoid arthritis.

This test has been developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared by the U.S. Food and Drug Administration.

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

The accuracy of genetic testing is not 100%. Results of genetic tests should be taken in the context of clinical representation and familial risk. The prevalence and significance of some allelic variations may be population specific.

Any positive findings in your patient's test indicate genetic predisposition that could affect physiologic function and risk of disease. We do not measure every possible genetic variation. Your patient may have additional risk that is not measured by this test. Negative findings do not imply that your patient is risk-free.

DNA sequencing is used to detect polymorphisms in the patient's DNA sample. The sensitivity and specificity of this assay is <100%.