

63 Zillicoa Street Asheville, NC 28801 © Genova Diagnostics

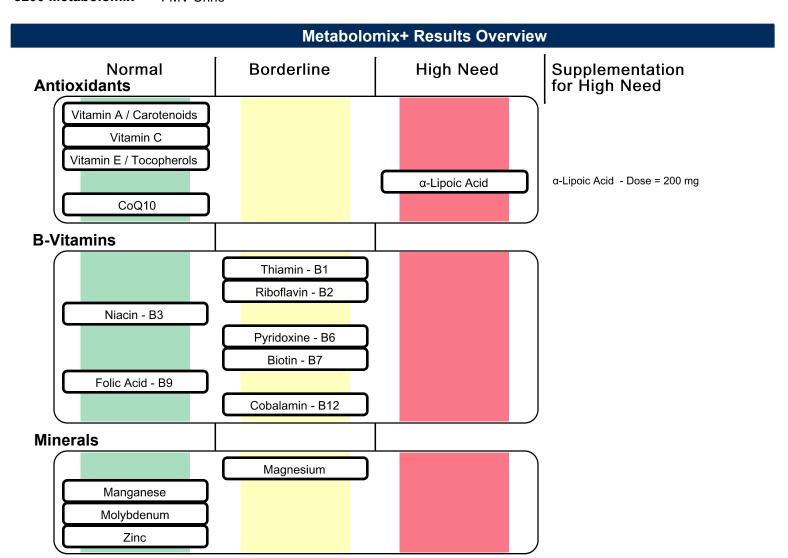


Patient: **SAMPLE**

PATIENT

DOB: Sex: MRN:

3200 Metabolomix+ - FMV Urine



SUGGESTED SUPPLEMENT SCHEDULE

| | Doily | LINEITI GOLLEGO | | |
|-------------------------|--------------------------------------|------------------------------------|--------------------------------|--|
| Supplements | Daily Recommended Intake (DRI) | Patient's Daily Recommendations | Provider Daily Recommendations | |
| Vitamin A / Carotenoids | 2,333 IU | 3,000 IU | | |
| Vitamin C | 75 mg | 250 mg | | |
| Vitamin E / Tocopherols | 22 IU | 100 IU | | |
| α-Lipoic Acid | | 200 mg | | |
| CoQ10 | | 30 mg | | |
| B-Vitamins | | | | |
| Thiamin - B1 | 1.1 mg | 25 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 | 200 mcg | | |
| Folic Acid - B9 | 400 mcg | 400 mcg | | |
| Cobalamin - B12 | 2.4 mcg | 500 mcg | | |
| Minerals | | | | |
| Magnesium | 320 mg | 600 mg | | |
| Manganese | 1.8 mg | 3.0 mg | | |
| Molybdenum | 45 mcg | 75 mcg | | |
| Zinc | 8 mg | 10 mg | | |
| Digestive Support | | | | |
| Probiotics | | 10 billion CFU | | |
| Pancreatic Enzymes | | 0 1U | | |
| Other Vitamins | | | | |
| Vitamin D | 600 IU | | | |
| Amino Acid | mg/day A | Amino Acid | mg/day | |
| Arginine | 0 N | 1ethionine | 404 | |
| Asparagine | 187 F | 187 Phenylalanine | | |
| Cysteine | 108 Serine | | 0 | |
| Glutamine | 89 Taurine | | 837 | |
| Glycine | 1,277 T | 1,277 Threonine | | |
| Histidine | 671 Tryptophan | | 0 | |
| Isoleucine | 0 Tyrosine 35 | | | |
| Leucine | 0 V | Valine 0 | | |
| Lysine | 494 | | | |

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.

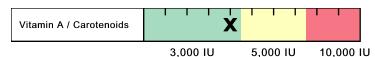
The Suggested Supplemental Schedule is provided at the request of the ordering practitioner. Any application of it as a therapeutic intervention is to be determined by the ordering practitioner.

| Key | Normal | Borderline | High Need |
|-----|--------|------------|-----------|
| Kev | | | |

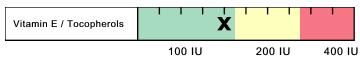
Metabolomix+ Interpretation At-A-Glance

Nutritional Needs

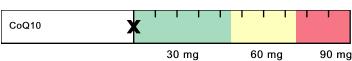
Antioxidants



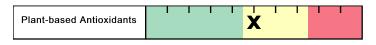
- Beta-carotene & other carotenoids are converted to vitamin A (retinol), involved in vision, antioxidant & immune function, gene expression & cell growth.
- Vitamin A deficiency may occur with chronic alcoholism, zinc deficiency, hypothyroidism, or oral contraceptives containing estrogen & progestin.
- 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.



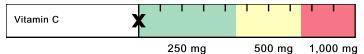
- Alpha-tocopherol (body's main form of vitamin E) functions as an antioxidant, regulates cell signaling, influences immune function and inhibits coagulation.
- Deficiency may occur with malabsorption, cholestyramine, colestipol, isoniazid, orlistat, olestra and certain anti-convulsants (e.g., phenobarbital, 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.



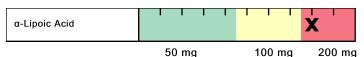
- CoQ10 is a powerful antioxidant that is synthesized in the body and contained in cell membranes. CoQ10 is also essential for energy production & pH regulation.
- CoQ10 deficiency may occur with HMG-CoA reductase inhibitors (statins), several anti-diabetic medication classes (biguanides, sulfonylureas) 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.



- 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 nutriceuticals (e.g., resveratrol, EGCG, lutein, lycopene, ginkgo, milk thistle, etc.).



- 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.



- 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 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.



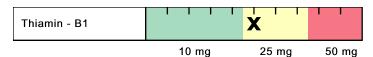
- Glutathione (GSH) is composed of cysteine, glutamine & glycine. GSH is a source of sulfate and plays a key role in antioxidant activity and detoxification of toxins.
- GSH requirement is increased with high-fat diets, cigarette smoke, cystinuria, chronic alcoholism, chronic acetaminophen use, infection,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

Key Function Causes of Deficiency Complications of Deficiency Food Sources

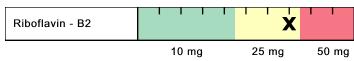
Metabolomix+ Interpretation At-A-Glance

Nutritional Needs

B-Vitamins



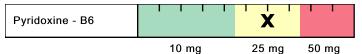
- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency 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.



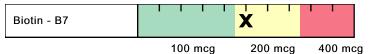
- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.
- 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.



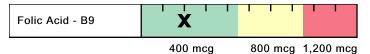
- ▶ B3 is used to form NAD and NADP, involved in energy production from food, fatty acid & cholesterol synthesis, cell signaling, DNA repair & cell differentiation.
- Low B3 may result from deficiencies of tryptophan (B3 precursor), B6, B2 or Fe (cofactors in B3 production), or from long-term isoniazid 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.



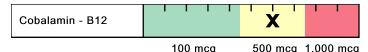
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or 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 is a cofactor for enzymes involved in functions such as fatty acid (FA) 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 use, 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.



- Folic acid 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.

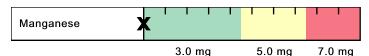


- B12 plays important roles in energy production from fats & proteins, methylation, synthesis of hemoglobin & RBCs, and maintenance of nerve cells, DNA & RNA.
- Low B12 may result from alcoholism, malabsorption, hypochlorhydria (e.g., from atrophic gastritis, H. pylori infection, pernicious anemia, H2 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.

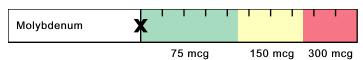
Metabolomix+ Interpretation At-A-Glance

Nutritional Needs

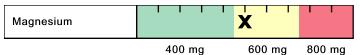
Minerals



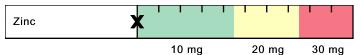
- Manganese plays an important role in antioxidant function, gluconeogenesis, the urea cycle, cartilage & bone formation, energy production and digestion.
- Impaired absorption of Mn may occur with excess intake of Fe, Ca, Cu, folic acid, or phosphorous compounds, or use of long-term TPN, Mg-containing 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 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).

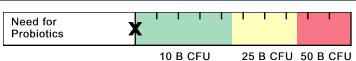


- Magnesium is involved in >300 metabolic reactions. Key areas include energy production, bone & ATP formation, muscle & nerve conduction and cell signaling.
- Deficiency may occur with malabsorption, alcoholism, hyperparathyroidism, renal disorders (wasting), diabetes, diuretics, digoxin or high doses 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.

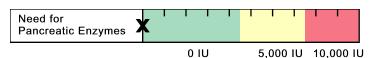


- Zinc plays a vital role in immunity, protein metabolism, heme synthesis, growth & development, reproduction, digestion and antioxidant function.
- Low levels may occur with malabsorption, alcoholism, chronic diarrhea, diabetes, excess Cu or Fe, diuretics, ACE inhibitors, H2 blockers or digoxin.
- Deficiency 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.

Digestive Support



- Probiotics have many functions. These include: production of some B vitamins and vitamin K; enhancement of digestion & absorption; decreasing severity of diarrheal illness; modulation 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.



- 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.

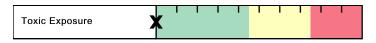
Page 6

Metabolomix+ Interpretation At-A-Glance

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.

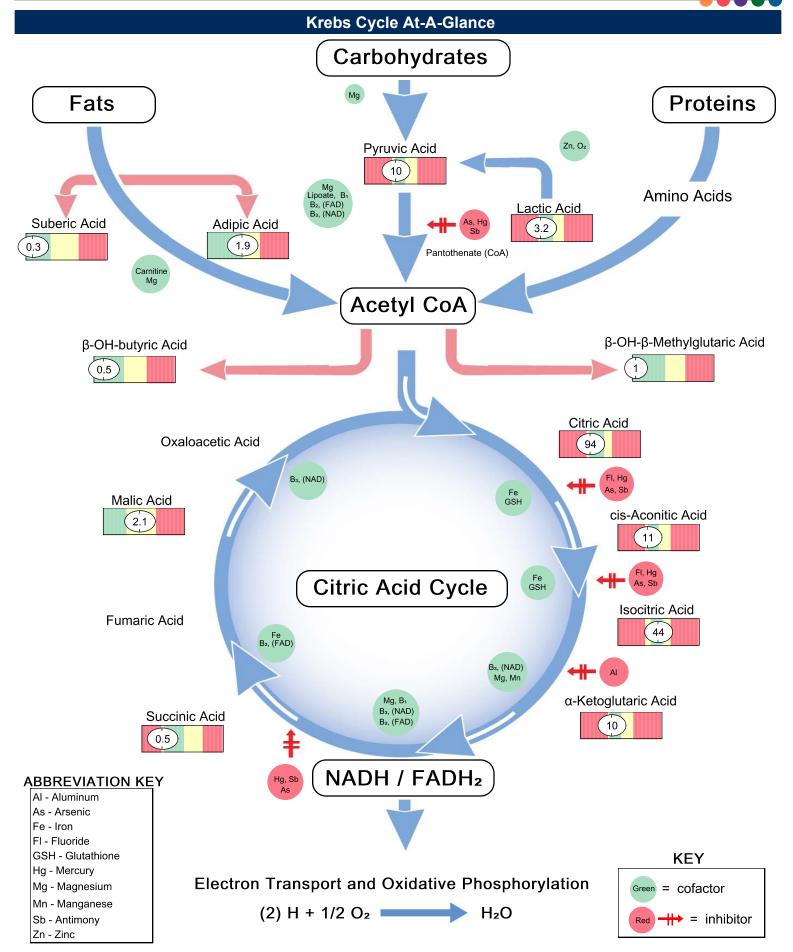


- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal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

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.





Metabolic Analysis Markers- FMV Urine

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

Malabsorption and Dysbiosis Markers

| Malabsorption Markers | | Refe | rence Range | |
|-----------------------------|------|------|-------------|--|
| Indoleacetic Acid (IAA) | 0.6 | | <= 4.2 | |
| Phenylacetic Acid (PAA) | 0.04 | | <= 0.12 | |
| Bacterial Dysbiosis Markers | | | | |

| Bacterial Dysbiosis Markers | | | | | | |
|---------------------------------------|-----|------|---------|--|--|--|
| Dihydroxyphenylpropionic Acid (DHPPA) | 0.3 | | <= 5.3 | | | |
| 3-Hydroxyphenylacetic Acid | 0.4 | | <= 8.1 | | | |
| 4-Hydroxyphenylacetic Acid | 2 | | <= 29 | | | |
| Benzoic Acid | | 0.05 | <= 0.05 | | | |
| Hippuric Acid | 1 | | <= 603 | | | |

Yeast / Fungal Dysbiosis Markers

| Arabinose | 1 | <= 96 |
|-----------------|-----|--------|
| Citramalic Acid | 0.4 | <= 5.8 |
| Tartaric Acid | 1 | <= 15 |

Cellular Energy & Mitochondrial Metabolites

| Carbohydrate Metabolism | | Refe | erence Range |
|--------------------------|-----|------|--------------|
| Lactic Acid | 3.2 | | 1.9-19.8 |
| Pyruvic Acid | 10 | | 7-32 |
| β-OH-Butyric Acid (BHBA) | 0.5 | | <= 2.8 |

Energy Metabolism

| 0,5 | | |
|----------------------------------|-----|---------|
| Citric Acid | 94 | 40-520 |
| Cis-Aconitic Acid | 11 | 10-36 |
| Isocitric Acid | 44 | 22-65 |
| α-Ketoglutaric Acid (AKG) | 10 | 4-52 |
| Succinic Acid | 0.5 | 0.4-4.6 |
| Malic Acid | 2.1 | <= 3.0 |
| β-OH-β-Methylglutaric Acid (HMG) | 1 | <= 15 |

Fatty Acid Metabolism

| Adipic Acid | 1.9 | <= 2.8 |
|--------------|-----|--------|
| Suberic Acid | 0.3 | <= 2.1 |

Creatinine Concentration

| \Box | ef | | | | _ | Г | _ | | | _ |
|--------|------------|----|----|----|-------------------|---|---|---|----|----------------|
| ĸ | ΔT | Δr | Δr | או | $\mathbf{\Delta}$ | ĸ | 9 | n | О. | $oldsymbol{a}$ |
| | | | | | | | | | | |

| Creatinine • | 8.8 | 3.1-19.5 mmol/L |
|--------------|-----|-----------------|

All biomarkers reported in mmol/mol creatinine unless otherwise noted

Neurotransmitter Metabolites

| | | Reference Range | | | |
|------------------------------|------|-----------------|--|--|--|
| Vanilmandelic Acid | 1.4 | 0.4-3.6 | | | |
| Homovanillic Acid | 1.6 | 1.2-5.3 | | | |
| 5-OH-indoleacetic Acid | 4.5 | 3.8-12.1 | | | |
| 3-Methyl-4-OH-phenylglycol | 0.15 | 0.02-0.22 | | | |
| Kynurenic Acid | 0.3 | <= 7.1 | | | |
| Quinolinic Acid | 0.3 | <= 9.1 | | | |
| Kynurenic / Quinolinic Ratio | 1.0 | >= 0.44 | | | |

Vitamin Markers

Reference Range

| Reference Na | | | | |
|--------------------------------|------|----|---------|--|
| α-Ketoadipic Acid | 0.4 | | <= 1.7 | |
| α-Ketoisovaleric Acid | 0.24 | | <= 0.97 | |
| α-Ketoisocaproic Acid | 0.8 | 37 | <= 0.89 | |
| α-Keto-β-Methylvaleric Acid | 0.4 | | <= 2.1 | |
| Formiminoglutamic Acid (FIGlu) | 0.7 | | <= 1.5 | |
| Glutaric Acid | 0.43 | | <= 0.51 | |
| Isovalerylglycine | 0.4 | | <= 3.7 | |
| Methylmalonic Acid | 0.5 | | <= 1.9 | |
| Xanthurenic Acid | 0.28 | | <= 0.96 | |
| 3-Hydroxypropionic Acid | 16 | | 5-22 | |
| 3-Hydroxyisovaleric Acid | 2 | | <= 29 | |

Toxin & Detoxification Markers

Reference Range

| α-Ketophenylacetic Acid (from Styrene) | 0.38 | <= 0.46 |
|--|------|-----------|
| α-Hydroxyisobutyric Acid (from MTBE) | 0.5 | <= 6.7 |
| Orotic Acid | 0.36 | 0.33-1.01 |
| Pyroglutamic Acid | 26 | 16-34 |

Tyrosine Metabolism

Reference Range

| Homogentisic Acid | 2 | <= 19 |
|----------------------------|------|---------|
| 2-Hydroxyphenylacetic Acid | 0.37 | <= 0.76 |

Metabolic Analysis Reference Ranges are Age Specific

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.

Amino Acids Analysis Markers - FMV Urine

Methodology: LC/MS/MS, Alkaline Picrate

Nutritionally Essential Amino Acids

| Amino Acid | | Refe | rence Range |
|---------------|-----|------|-------------|
| Arginine | 19 | | 3-43 |
| Histidine | 163 | | 124-894 |
| Isoleucine | 19 | | 3-28 |
| Leucine | 26 | | 4-46 |
| Lysine | 29 | | 11-175 |
| Methionine | 3 | | 2-18 |
| Phenylalanine | 23 | | 8-71 |
| Taurine | 31 | | 21-424 |
| Threonine | 69 | | 17-135 |
| Tryptophan | 19 | | 5-53 |
| Valine | 33 | | 7-49 |

Nonessential Protein Amino Acids

| Amino Acid | F | Refe | rence Range |
|----------------------|-----|------|-------------|
| Alanine | 63 | | 63-356 |
| Asparagine | 40 | | 25-166 |
| Aspartic Acid | 13 | | <= 14 |
| Cysteine (FMV urine) | 16 | | 8-74 |
| Cystine (FMV Urine) | 19 | | 10-104 |
| γ-Aminobutyric Acid | 3 | | <= 5 |
| Glutamic Acid | 15 | | 4-27 |
| Glutamine | 188 | | 110-632 |
| Proline | 6 | | 1-13 |
| Tyrosine | 30 | | 11-135 |

Creatinine Concentration





Amino Acid reference ranges are age specific.

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.

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

Intermediary Metabolites

| B Vitamin Markers | F | Refe | rence Range |
|------------------------|----|------|-------------|
| α-Aminoadipic | 19 | | 2-47 |
| α-Amino-N-butyric Acid | 15 | | 2-25 |
| β-Aminoisobutyric Acid | 16 | | 11-160 |
| Cystathionine | 15 | | 2-68 |
| 3-Methylhistidine | 50 | | 44-281 |

Urea Cycle Markers

| Citrulline | 1.3 | 0.6-3.9 |
|------------|-----|------------------------------|
| Ornithine | 15 | 2-21 |
| Urea ◆ | 357 | 168-465 mmol/g creatinine |

Glycine/Serine Metabolites

| • | | |
|---------------------|-----|--------|
| Glycine | 138 | 95-683 |
| Serine | 69 | 40-163 |
| Ethanolamine | 73 | 50-235 |
| Phosphoethanolamine | 4 | 1-13 |
| Phosphoserine | 6 | 3-13 |
| Sarcosine | 0.5 | <= 1.1 |

Dietary Peptide Related Markers

Reference Range

| Anserine (dipeptide) | 18.8 | 0.4-105.1 |
|-----------------------|------|-----------|
| Carnosine (dipeptide) | 15 | 1-28 |
| 1-Methylhistidine | 45 | 38-988 |
| β-Alanine | 15 | <= 22 |

Oxidative Stress Markers - FMV Urine

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

Oxidative Stress Markers

Reference Range

| Lipid Peroxides (urine) | 8.3 | <=10.0 micromol/g Creat. |
|-------------------------|-----|-----------------------------|
| 8-OHdG (urine) | 5 | <=15 mcg/g Creat. |

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.

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

Methodology: GCMS

| Omega 3 Fatty Acids | | | |
|---|------|-------------------|--|
| Analyte (cold water fish, flax, walnut) Reference Range | | | |
| α-Linolenic (ALA) 18:3 n3 | | 1.22 >= 0.09 wt % | |
| Eicosapentaenoic (EPA) 20:5 n3 | | 1.22 >= 0.12 wt % | |
| Docosapentaenoic (DPA) 22:5 n3 | 1.22 | >= 0.34 wt % | |
| Docosahexaenoic (DHA) 22:6 n3 | 1.2 | >= 0.8 wt % | |
| % Omega 3s | 4.9 | >= 1.6 | |

| Omega 9 Fatty Acids | | | | |
|-------------------------------------|------|--------------|--|--|
| Analyte (olive oil) Reference Range | | | | |
| Oleic 18:1 n9 | 15 | 14-21 wt % | | |
| Nervonic 24:1 n9 | 1.2 | 1.1-1.8 wt % | | |
| % Omega 9s | 17.1 | 17.3-22.5 | | |

| Saturated Fatty Acids | | | | |
|--|---|------|-----------------|----------------|
| Analyte (meat, dairy, coconuts, palm oils) Reference Range | | | deference Range | |
| Palmitic C16:0 | | 26 | | 19-27 wt % |
| Stearic C18:0 | | 10 | | 9-12 wt % |
| Arachidic c20:0 | | 0.37 | | 0.24-0.40 wt % |
| Behenic C22:0 | | 1.22 | | 0.92-1.68 wt % |
| Tricosanoic c23:0 | | 0.24 | | 0.19-0.26 wt % |
| Lignoceric c24:0 | (| 1.2 | | 1.1-1.9 wt % |
| Pentadecanoic c15:0 | | 0.24 | | 0.14-0.30 wt % |
| Margaric C17:0 | | 0.37 | | 0.24-0.45 wt % |
| % Saturated Fats | 3 | 9.1 | | 39.8-43.6 |

| Omega 6 Fatty Acids | | | |
|--------------------------------------|------------------------|-----------------|--|
| Analyte (vegetable oil, grain | ns, most meats, dairy) | Reference Range | |
| Linoleic (LA) 18:2 n6 | 24.4 | 18.8-28.3 wt % | |
| y-Linolenic (GLA) 18:3 n6 | 0.37 | 0.15-0.54 wt % | |
| Dihomo-γ-linolenic (DGLA) 20:3 n6 | 2.44 | >= 1.19 wt % | |
| Arachidonic (AA) 20:4 n6 | 7 | 7-12 wt % | |
| Docosatetraenoic (DTA) 22:4 n6 | 1.22 | 0.45-1.25 wt % | |
| Eicosadienoic 20:2 n6 | 0.24 | <= 0.26 wt % | |
| % Omega 6s | 36.0 | 30.5-39.7 | |

| Monounsaturated Fats | | | |
|----------------------|------|---|----------------|
| Omega 7 Fats | | R | eference Range |
| Palmitoleic | 1.22 | | <= 2.58 wt % |
| Vaccenic 18:1 n7 | 1.22 | | <= 1.65 wt % |
| Trans Fat | | | |
| Elaidic 18:1 n9t | 0.49 |) | <= 0.59 wt % |

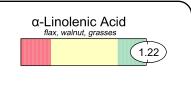
| Delta - 6 Desaturase Activity | | |
|--------------------------------------|---------------------------------|-----------|
| | Upregulated Functional Impaired | i |
| Linoleic / DGLA 18:2 n6 / 20:3 n6 | 10.0 | 12.6-31.5 |

| Cardiovascular Risk | | | |
|-------------------------------|-----|-----------------|--|
| Analyte | R | Reference Range | |
| Omega 6s / Omega 3s | 7.4 | 8.5-27.4 | |
| AA / EPA 20:4 n6 / 20:5 n3 | 6 | 10-86 | |
| Omega 3 Index | 9.2 | >= 4.0 | |

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

Essential Fatty Acid Metabolism

Omega 3 Family



Stearidonic acid

Eicosatetraenoic acid, ETA

Eicosapentaenoic Acid cold water fish 1.22 Anti-inflammatory Eicosanoids

Docosapentaenoic Acid

Docosahexaenoic Acid

Delta-6 Desaturase

Vitamin and Mineral Cofactors:

FAD (B2), Niacin (B3) Pyridoxal-5-phosphate (B6) Vitamin C, Insulin, Zn, Mg

Elongase

Vitamin and Mineral Cofactors:

Niacin (B3) Pyridoxal-5-phosphate (B6) Pantothenic Acid (B5) Biotin, Vitamin C

Delta-5 Desaturase Vitamin and Mineral Cofactors:

FAD (B2), Niacin (B3) Pyridoxal-5-phosphate (B6) Vitamin C, Insulin, Zn, Mg

Elongase

Vitamin and Mineral Cofactors:

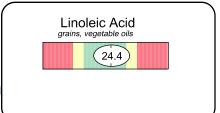
Niacin (B3) Pyridoxal-5-phosphate (B6), Biotin Pantothenic Acid (B5), Vitamin C

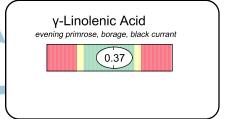
Elongase Delta-6 Desaturase

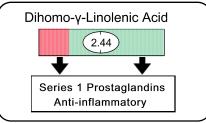
Vitamin and Mineral Cofactors:

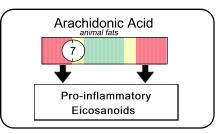
FAD (B2), Niacin (B3) Pyridoxal-5-phosphate (B6), Biotin Vitamin C, Zn, Mg, Carnitine Pantothenic Acid (B5)

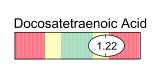
Omega 6 Family











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

3204 Add-on Comprehensive Urine Elements - FMV Urine

Methodology: ICP-MS and Alkaline Picrate

| Toxic Elements | | | |
|----------------|----------------------|--------------------------------|----------|
| Element R | Results Reference | in ug/g creatinin Range TMP | |
| Lead | 1.0 |) | <= 1.4 |
| Mercury | 0.50 | | <= 2.19 |
| Aluminum | 2.5 | | <= 22.3 |
| Antimony | 0.025 | | <= 0.149 |
| Arsenic | 1 | | <= 50 |
| Barium | 0.5 | | <= 6.7 |
| Bismuth | 0.75 | | <= 2.28 |
| Cadmium | 0.25 | | <= 0.64 |
| Cesium | 2.5 | | <= 10.5 |
| Gadolinium | 0.010 | | <= 0.019 |
| Gallium (| 0.003 | | <= 0.028 |
| Nickel | 2.50 |) | <= 3.88 |
| Niobium | 0.040 | | <= 0.084 |
| Platinum | 0.015 | | <= 0.033 |
| Rubidium | 3 | | <= 2,263 |
| Thallium | 0.050 | | <= 0.298 |
| Thorium | 2.500 |) | <= 4.189 |
| Tin (| 0.10 | | <= 2.04 |
| Tungsten | 0.025 | | <= 0.211 |
| Uranium | 0.010 | | <= 0.026 |

| Nutrient Elements | | | |
|-------------------|---|----|--------------------|
| Element | Results in ug/g creatinine Reference Range | | Reference Range |
| Chromium | 2.5 | | 0.6-9.4 |
| Cobalt | 2.5 | 50 | 0.01-2.60 |
| Copper | 5.0 | | 4.0-11.4 |
| Iron | 10 | | 5-64 |
| Lithium | 25 | | 9-129 |
| Manganese | 0.25 | | 0.03-1.16 |
| Molybdenum | 25 | | 15-175 |
| Selenium | 180 | | 32-333 |
| Strontium | 125 | | 47-346 |
| Vanadium | 2.5 | | 0.1-3.2 |
| Zinc | 250 | | 63-688 |

| | tinine Reference | |
|-----------|------------------|-----------|
| Element | Reference Rang | e Range |
| Calcium | 40 | 37-313 |
| Magnesium | 48 | 41-267 |
| Potassium | 2,550 | 759-4,653 |
| Sulfur | 390 | 367-1,328 |

Creatinine Concentration

Urine Creatinine

100.00

23.00-205.00 mg

Genomic Results



63 Zillicoa Street Asheville, NC 28801 © Genova Diagnostics

Patient: SAMPLE PATIENT

DOB: Sex: MRN:

Apo E

Apolipoprotein E : CHOLESTEROL REGULATION

Location: Chromosome 19 **APOF**

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

Health Implications

- The E2/E4 genotype is rare, accounting for less than 3% of a given population.
- · ApoE4 confers a tendency toward higher total- and LDL-cholesterol and lower HDL-C; ApoE2 is associated with the opposite trend but also with higher triglycerides (TGs).
- · Although E2 is generally protective, E4 confers increased risk of atherosclerosis, MI, oxidative stress, stroke (and cognitive impairment after stroke), osteoporosis, and toxicity by heavy metals such as lead and mercury.
- E2 confers a slightly increased risk of type 2 diabetes and diabetic nephropathy.

Clinical Management Considerations

- · Restriction of saturated fat and cholesterol lowers total- and LDL cholesterol and CAD risk the most effectively in ApoE4 individuals.
- · Minimize sugar and high-glycemic index foods, which produce the largest TG response in E2 carriers; also reduce excess weight, which synergizes with effects of E4 on lipids and insulin.
- · Fish oils help to lower TGs, but may also increase LDL-C in E4 carriers; good lipid response to dietary
- · Alcohol may have mixed effects in men (may reduce LDL-C in E2 carriers, but may raise LDL-C and IL-6 levels in E4 carriers).
- · Anti-inflammatory agents may help preserve cognitive function.
- · Lipid response to statins, and TG response to fibrates, are usually the best in E2 > E3 > E4; studies are mixed.
- · Gemfibrozil helps reduce total cholesterol and TGs in E2 individuals.
- · Estrogen therapy is particularly efficacious for both cholesterol and bone in postmenopausal E4 carriers, although oral forms may increase TGs in E2 carriers.

Kev

Neither chromosome carries the genetic variation.

One chromosome (of two) carries the genetic variation. + + Both chromosomes carry the genetic variation.

Gene activity increased Gene activity decreased

(You inherit one chromosome from each parent)





MTHFR 5,10-methyltetrahydrofolate reductase: METHYLATION 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. Location: Chromosome 1 **Health Implications** C677T · Homozygosity for 1298 (+/+) results in 30-40% reduction in MTHFR enzyme activity, which may Your Genotype: moderately limit methylation reactions in the body; effect is mild compared to the C677T polymorphism · High homocysteine and disease risks are primarily associated with the C677T (+/+) genotype Some studies indicate possible increased risks of male infertility, ischemic stroke and hepatocellular carcinoma in Asians, and congenital heart defects in Caucasian children A1298C **Clinical Management Considerations** Your Genotype: · Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods · Consider supplementation with folic acid (or 5-methyl tetrahydrofolate, which bypasses the MTHFR step), B2, B6 (pyridoxal 5-phosphate), B12 (or methylcobalamin), and betaine (trimethylglycine)



COMT

Catechol-O-MethylTransferase: METHYLATION

Location: Chromosome 22.11q V158M Your Genotype:

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 various chemicals and toxins, such as aryl hydrocarbons.

Health Implications

- · Most common genotype in individuals of European descent
- · Moderately reduced COMT enzyme activity, resulting in slightly impaired methylation
- · Strong cognitive stability, e.g., ability to focus (due to higher brain dopamine) but lower cognitive flexibility (e.g., ability to adapt to external changes), compared to the (-/-) genotype
- · Cognitive benefit may increase as dopamine levels decline with age

ID:

- · Acute or chronic stress may increase risk of nervousness and anxiety (esp. when history of childhood trauma), due to higher baseline levels of catecholamines
- · Past studies have suggested increased breast cancer risk under certain conditions; however, larger and more recent studies have not confirmed these findings
- · Moderately reduced pain threshold, exacerbated by one's experience of pain; slightly increased risk of fibromyalgia and chronic pain syndromes

Clinical Management Considerations

- · Ensure adequate B6, B12, folate, magnesium, and methionine to support formation of S-adenosylmethionine and prevent elevated homocysteine; S-adenosylhomocysteine inhibits COMT
- · Exercise caution using conjugated equine estrogens such as Premarin®; in-vitro studies suggest show one of its metabolites to inhibit COMT
- · Individuals with this genotype might have a superior response to SSRI antidepressants (mixed studies)
- · In children with ADHD, methylphenidate (Ritalin®) may be less effective (mixed studies)

© Genova Diagnostics · A. L. Peace-Brewer, PhD, D(ABMLI) interated · CLIA Lic. #34D0655571 · Medicare Lic. #34-8475

Patient: SAMPLE PATIENT



TNF-α Tumor Necrosis Factor-alpha: INFLAMMATION TNF-alpha (TNF- α) is a pro-inflammatory cytokine secreted that is secreted from activated macrophages. TNF- α 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- α medications (e.g., etanercept) in rheumatoid arthritis.

ID: