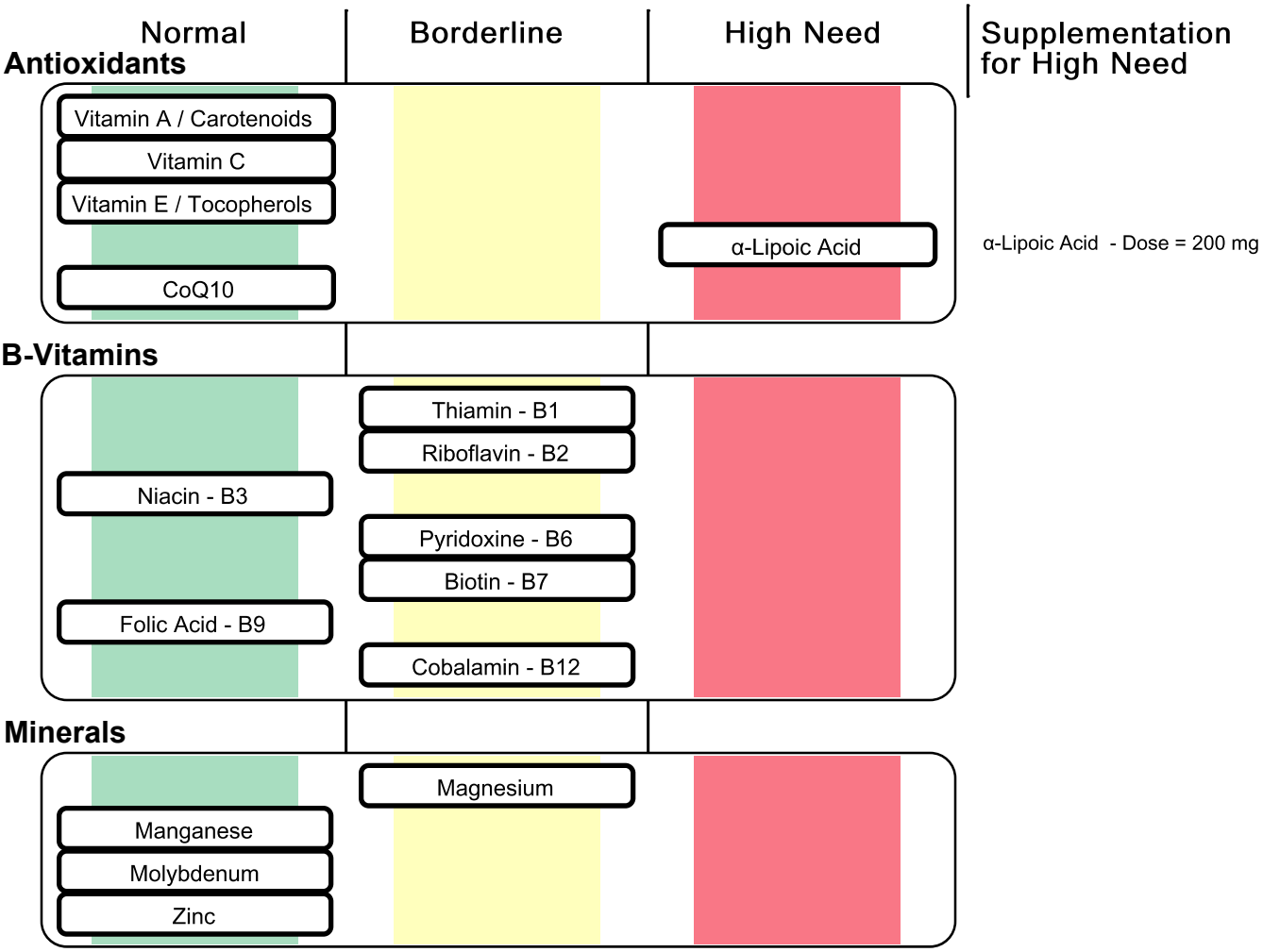
GENOVA DIAGNOSTICS
63 Zillicoa Street
Asheville, NC 28801

Metabolomix+

Patient: **SAMPLE PATIENT**
DOB:
Sex:
MRN:

3200 Metabolomix+ - FMV Urine

Metabolomix+ Results Overview



SUGGESTED SUPPLEMENT SCHEDULE

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
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 IU	
Other Vitamins			
Vitamin D	600 IU		

Amino Acid	mg/day	Amino Acid	mg/day
Arginine	0	Methionine	404
Asparagine	187	Phenylalanine	0
Cysteine	108	Serine	0
Glutamine	89	Taurine	837
Glycine	1,277	Threonine	0
Histidine	671	Tryptophan	0
Isoleucine	0	Tyrosine	35
Leucine	0	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

Metabolomix+ Interpretation At-A-Glance

Nutritional Needs

Antioxidants

Vitamin A / Carotenoids

- 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

- 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.

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

Key

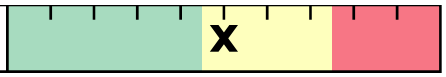
- Function
- Causes of Deficiency
- Complications of Deficiency
- Food Sources

Metabolomix+ Interpretation At-A-Glance

Nutritional Needs

B-Vitamins

Thiamin - B1

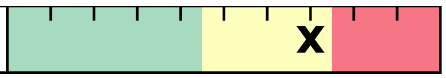


- B1 is a required cofactor for enzymes involved in energy production from food, and for the synthesis of ATP, GTP, DNA, RNA and NADPH.
- Low B1 can result from chronic alcoholism, diuretics, digoxin, oral contraceptives and HRT, or large amounts of tea & coffee (contain anti-B1 factors).
- B1 deficiency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

Pyridoxine - B6

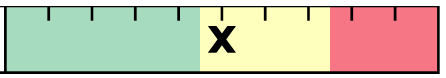
- B6 (as P5P) is a cofactor for enzymes involved in glycogenolysis & gluconeogenesis, and synthesis of neurotransmitters, heme, B3, RBCs and nucleic acids.
- Low B6 may result from chronic alcoholism, long-term diuretics, estrogens (oral contraceptives and HRT), anti-TB meds, penicillamine, L-DOPA or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

Riboflavin - B2



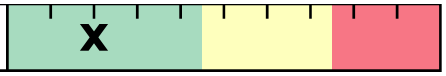
- B2 is a key component of enzymes involved in antioxidant function, energy production, detoxification, methionine metabolism and vitamin activation.
- Low B2 may result from chronic alcoholism, some anti-psychotic medications, oral contraceptives, tricyclic antidepressants, quinacrine or adriamycin.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

Biotin - B7



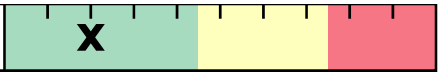
- Biotin is a cofactor for enzymes involved in functions such as fatty acid (FA) synthesis, mitochondrial FA oxidation, gluconeogenesis, and DNA replication & transcription.
- Deficiency may result from certain inborn errors, chronic intake of raw egg whites, long-term TPN use, anticonvulsants, high-dose 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.

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.

Folic Acid - B9



- 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.

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.

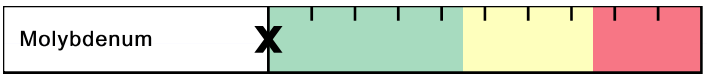
Metabolomix+ Interpretation At-A-Glance

Nutritional Needs

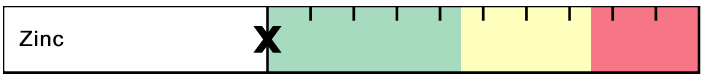
Minerals

- 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.

- 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 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 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.

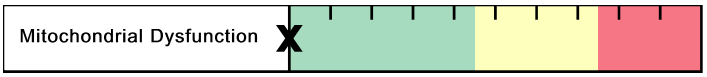
Digestive Support

- 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.

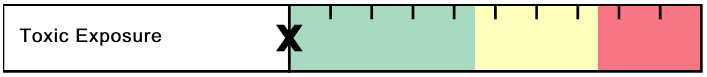
- Pancreatic enzymes are secreted by the exocrine glands of the pancreas and include protease/peptidase, lipase and amylase.
- Pancreatic exocrine insufficiency may be primary or secondary in nature. Any indication of insufficiency warrants further evaluation for underlying cause (i.e., celiac disease, 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.

Metabolomix+ Interpretation At-A-Glance

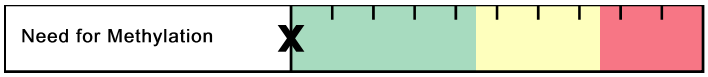
Functional Imbalances



- 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.

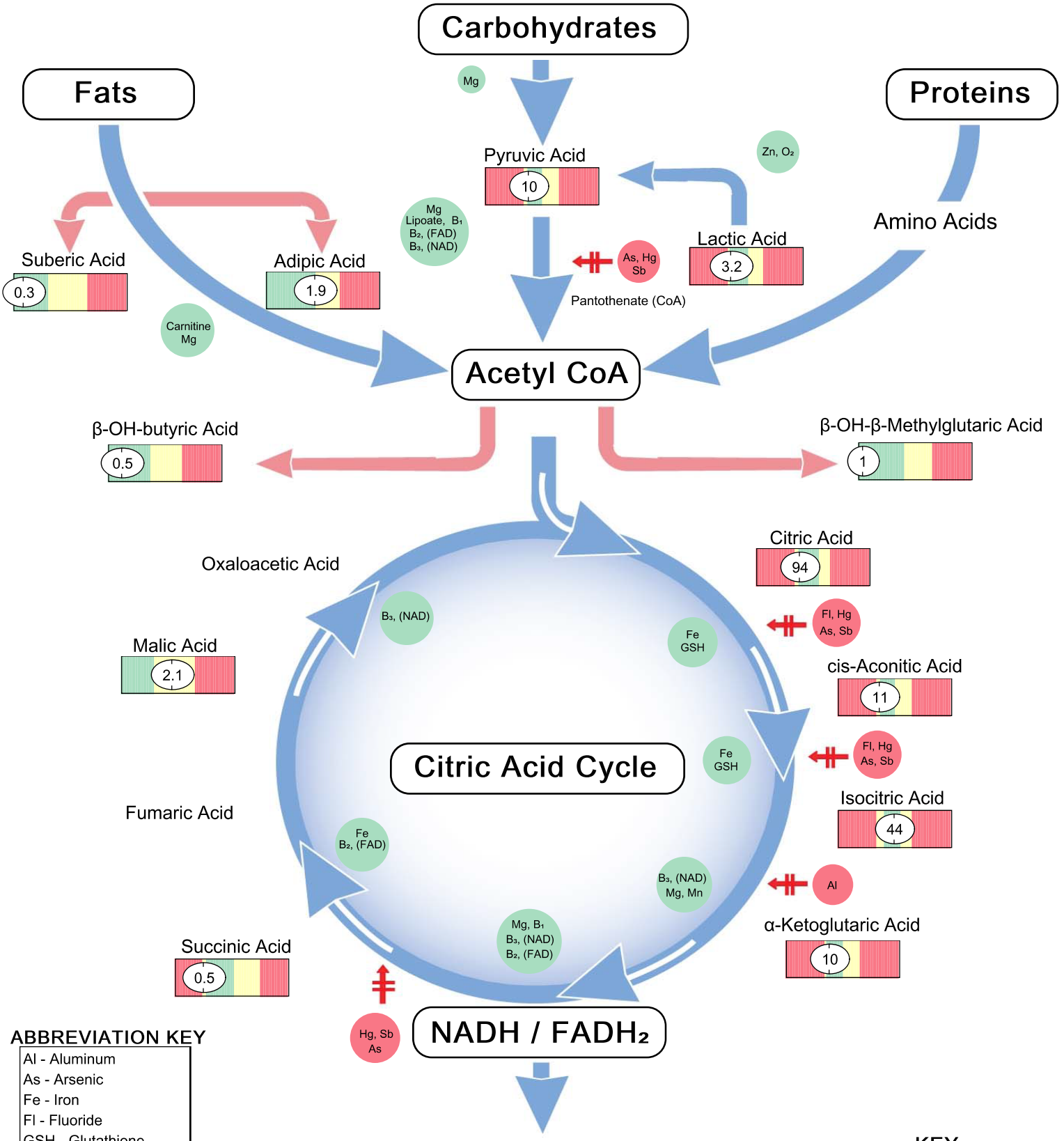


- Methyl tert-Butyl Ether (MTBE) is a common gasoline additive used to increase octane ratings, and has been found to contaminate ground water supplies where gasoline is stored. Inhalation of MTBE may cause nose and throat irritation, as well as headaches, nausea, dizziness and mental confusion. Animal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



- 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.

Krebs Cycle At-A-Glance



ABBREVIATION KEY

Al - Aluminum
As - Arsenic
Fe - Iron
Fl - Fluoride
GSH - Glutathione
Hg - Mercury
Mg - Magnesium
Mn - Manganese
Sb - Antimony
Zn - Zinc

KEY

Green = cofactor

Red = inhibitor

Metabolic Analysis Markers- FMV Urine

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

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

Malabsorption and Dysbiosis Markers

Malabsorption Markers

	Reference Range
Indoleacetic Acid (IAA)	<= 4.2
Phenylacetic Acid (PAA)	<= 0.12

Bacterial Dysbiosis Markers

	Reference Range
Dihydroxyphenylpropionic Acid (DHPPA)	<= 5.3
3-Hydroxyphenylacetic Acid	<= 8.1
4-Hydroxyphenylacetic Acid	<= 29
Benzoic Acid	<= 0.05
Hippuric Acid	<= 603

Yeast / Fungal Dysbiosis Markers

	Reference Range
Arabinose	<= 96
Citramalic Acid	<= 5.8
Tartaric Acid	<= 15

Cellular Energy & Mitochondrial Metabolites

Carbohydrate Metabolism

	Reference Range
Lactic Acid	1.9-19.8
Pyruvic Acid	7-32
β-OH-Butyric Acid (BHBA)	<= 2.8

Energy Metabolism

	Reference Range
Citric Acid	40-520
Cis-Aconitic Acid	10-36
Isocitric Acid	22-65
α-Ketoglutaric Acid (AKG)	4-52
Succinic Acid	0.4-4.6
Malic Acid	<= 3.0
β-OH-β-Methylglutaric Acid (HMG)	<= 15

Fatty Acid Metabolism

	Reference Range
Adipic Acid	<= 2.8
Suberic Acid	<= 2.1

Creatinine Concentration

	Reference Range
Creatinine ◆	3.1-19.5 mmol/L

Neurotransmitter Metabolites

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

Vitamin Markers

	Reference Range
α-Ketoadipic Acid	<= 1.7
α-Ketoisovaleric Acid	<= 0.97
α-Ketoisocaproic Acid	<= 0.89
α-Keto-β-Methylvaleric Acid	<= 2.1
Formiminoglutamic Acid (FIGlu)	<= 1.5
Glutaric Acid	<= 0.51
Isovalerylglycine	<= 3.7
Methylmalonic Acid	<= 1.9
Xanthurenic Acid	<= 0.96
3-Hydroxypropionic Acid	5-22
3-Hydroxyisovaleric Acid	<= 29

Toxin & Detoxification Markers

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

Tyrosine Metabolism

	Reference Range
Homogentisic Acid	<= 19
2-Hydroxyphenylacetic Acid	<= 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

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

Nutritionally Essential Amino Acids

Amino Acid		Reference 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		Reference 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

		Reference Range
Creatinine ◆	7.1	3.1-19.5 mmol/L

Amino Acid reference ranges are age specific.

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Intermediary Metabolites

B Vitamin Markers		Reference 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
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	39.1	39.8-43.6

Omega 6 Fatty Acids

Analyte (vegetable oil, grains, most meats, dairy)		Reference Range
Linoleic (LA) 18:2 n6	24.4	18.8-28.3 wt %
γ-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		Reference Range
Palmitoleic 16:1 n7	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	
Linoleic / DGLA 18:2 n6 / 20:3 n6	10.0	12.6-31.5

Cardiovascular Risk

Analyte		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

α-Linolenic Acid
flax, walnut, grasses
1.22

Stearidonic acid

Eicosatetraenoic acid, ETA

Eicosapentaenoic Acid
cold water fish
1.22
Anti-inflammatory Eicosanoids

Docosapentaenoic Acid
1.22

Docosahexaenoic Acid
cold water fish
1.2

Omega 6 Family

Linoleic Acid
grains, vegetable oils
24.4

γ-Linolenic Acid
evening primrose, borage, black currant
0.37

Dihomo-γ-Linolenic Acid
2.44
Series 1 Prostaglandins Anti-inflammatory

Arachidonic Acid
animal fats
7
Pro-inflammatory Eicosanoids

Docosatetraenoic Acid
1.22

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)

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	Results in ug/g creatinine (Reference Range / TMPL)	Reference Range
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	2.50	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

Element	Results in mg/g creatinine (Reference Range)	Reference 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

GENOVATIONS™

63 Zillicoa Street
Asheville, NC 28801

Patient: SAMPLE PATIENT

DOB:
Sex:
MRN:

Apo E

Location:
Chromosome 19
APOE
APO E2: cys / cys
APO E3: cys / arg
APO E4: arg / arg
Your Genotype:

2	4

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 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 fiber.
- 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.

Key

- - 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

GENOVA DIAGNOSTICS

MTHFR	5,10-methyltetrahydrofolate reductase : METHYLATION
Location: Chromosome 1 C677T Your Genotype:	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.
	**Health Implications** · Homozygosity for 1298 (+/+) results in 30-40% reduction in MTHFR enzyme activity, which may 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 Your Genotype:	**Clinical Management Considerations** · 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
- 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)

TNF-α	Tumor Necrosis Factor-alpha: INFLAMMATION
Location: Chromosome 6 -308G-A Your Genotype:	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 inflammation and oxidative stress.

Health Implications

- Decreased production of TNF-α, decreased inflammatory tendency and oxidative stress compared to the other 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.

Metabolomix+

BEFORE YOU BEGIN:

There are multiple samples requested for this testing and you will notice multiple collection containers. This page is designed to provide a high level overview of the collection process and requirements while each bag will contain very specific and detailed instructions.

IMPORTANT THINGS TO KNOW AND CONSIDER

- **Testing is not available for patients less than 2 years old**
- **Female patients should not collect during menstrual period**

2 Days before the test

- **Discontinue** all of the following (unless instructed otherwise by your physician):
  - » **Supplements containing creatine, vitamin C or any mineral elements** measured on this test
  - » **Other substances that may influence urinary element excretion of elements**
  - » **Seafood** (unless asked to continue by your healthcare provider)
  - » **Continue** with the above food restrictions until your sample is completely collected

24 hrs before the test:

- **Eat** usual diet, but **avoid** over-consuming any single food or extreme diet
- Fluid intakes should be **limited to eight (8) 8-ounce glasses of fluid over a 24 hour period**

BAG ONE contains the collection instructions supplies needed to collect a
Blood Spot Essential & Metabolic Fatty Acid Profile
(note this may or may not be requested by your Health Care Provider, please see requisition form to determine if this collection is necessary. This is typically collected the morning of Day 1 and requires an 8 hour fast)

BAG TWO contains the collection instructions and supplies needed to collect urine specimens for a **Metabolomix+**
*(note this requires an 8 hour fast and is typically collected the morning of Day 2) as well as collection instructions and supplies needed to collect a **buccal swab for genetic markers** (note this may or not be requested by your Health Care Provider, **please see requisition form to determine if this collection is necessary**.*
This is also typically collected the morning of Day 2)

GENOVA DIAGNOSTICS®

Call 800.522.4762 or visit our website at www.gdx.net

ENSURE THE FOLLOWING:

Blood spot card

- ❑ First and last name and date of collection are written on the bloodspot card
- ❑ Placed in resealable plastic bag with desiccant/moisture absorbent pack
- ❑ Completely dried (apprx 24 hours)

All required information:

Can be completed online or using included paper forms

- ❑ All sections of **test requisition form** completed
- ❑ **Payment information provided**

❑ **All tubes, the card, and associated forms** placed back in the original Genova sample collection pack box prior to shipping

SHIP THE SAMPLE(S) TO THE LAB

Ship only Monday through Friday, and within 24 hours after final collection.
Please refer to the shipping instruction insert found in your Genova sample collection pack box.

REGISTER FOR THE PATIENT RESOURCE CENTER AT WWW.GDX.NET/PRC

- Complete health surveys
- Make payments
- Access test results

GENOVA DIAGNOSTICS

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Metabolomix+ BAG ONE COLLECTION

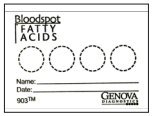
PATIENT SAMPLE COLLECTION INSTRUCTIONS FOR THE FOLLOWING PROFILE

Metabolomix+ *

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

BAG ONE COLLECTION MATERIALS FOR SAMPLE

Lancets (2)



Bloodspot card

REQUIRED MATERIALS

- Alcohol prep pad (2)
- Adhesive bandage
- Absorbent pad
- Resealable plastic bag with desiccant/moisture absorbent pack
- Genova sample collection pack box
- FedEx® Clinical Lab Pak and Billable Stamp

IMPORTANT PREP BEFORE PATIENT TAKES TEST

Night before the test

- Patients must fast overnight prior to collecting the bloodspot

PLEASE READ THE BEFORE YOU BEGIN SHEET INCLUDED BEFORE PROCEEDING TO COLLECTION

K-GDX-103

* Not available in New York

If any items are missing or expired, or liquid is spilled, call Client Services at 800.522.4762 and press "1"

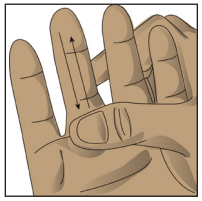
BLOOD SPOT COLLECTION

1. **Write first and last name** and **date of collection** on the blood spot card

2. **Wash** hands with warm water for a minimum of 20 seconds. **Dry** hands.

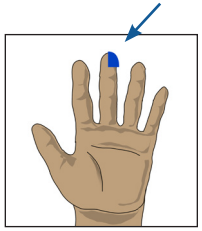
To improve circulation;

- **Hold** your hand lower than heart level and **gently massage** the entire length the middle finger for 30 seconds.
- Firmly **grasp** the top knuckle of the middle finger for a few seconds to restrict return circulation.
- **Hang** arm down and **gently shake** your fingers a few seconds to increase blood pools in the finger.

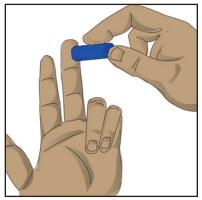


3. **Clean** the tip of your finger with the alcohol pad.

4. **Remove** the clear cover from the lancet. One end of the lancet has a small hole in the center; this will be the end that you press firmly against your finger to engage the lancet.

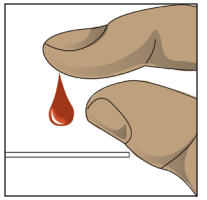


5. **Locate** the appropriate site on the middle fingertip (see image).



6. **Place** the hole-end of the lancet firmly against your fingertip to **depress** the tip and release the lancet. The lancet will immediately retract safely after depression.

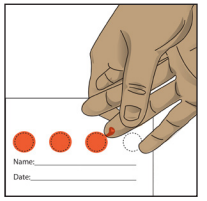
7. Using your thumb, **gently massage** entire length of the pricked finger to form repeated blood drops. As each drop forms, touch the tip of the drop to a circle on the collection card. **Do not smear. Do NOT touch fingertip to card!!**



8. **Repeat** until blood **has soaked to the border of the circle** on the collection card. Continue this procedure for all four circles.

If you are unable to get enough blood from the first collection, repeat this procedure with a different finger.

If necessary, use the absorbent pad to dry the site on your finger after your collection. Use the enclosed adhesive bandage as needed.



9. **Allow** absorbent collection card to air dry overnight, **approximately 24 hours, before placing in the resealable plastic bag** with desiccant/moisture absorbent pack for shipping. **If the card is not completely dry, your sample may be unusable.**

AVOID:	CONFIRM:
Layering blood on a previously dried spot	Blood should saturate through both sides of the card
Smearing blood onto the card	Requisition is properly completed and signed
Touching the surface of the card with fingers	Dried card is in zip lock bag with desiccant
ACCEPTABLE COLLECTION CARD EXAMPLE	UNACCEPTABLE COLLECTION CARD EXAMPLE:
	

ENSURE THE FOLLOWING:

❑ **Labels completed** with **patient's date of birth** are on all tubes as well as the test requisition form

All tubes:

❑ Are tightly closed

❑ Sealed in the biohazard bag with absorbent pad

❑ Frozen until packaged for shipping

Swabs (ONLY FOR GENOMICS ADD-ONS):

❑ Swabs in the package and in the envelope

All required information:

Can be completed online or using included paper forms

❑ All sections of **test requisition form** completed

❑ **Payment information provided**

❑ **All tubes and associated forms** placed back in the original Genova sample collection pack box prior to shipping

SHIP THE SAMPLE(S) TO THE LAB

Ship only Monday through Friday, and within 24 hours after final collection.
Please refer to the shipping instruction insert found in your Genova sample collection pack box.

REGISTER FOR THE PATIENT RESOURCE CENTER AT WWW.GDX.NET/PRC

- Complete health surveys
- Make payments
- Access test results

GENOVA DIAGNOSTICS

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K-103

Metabolomix+ BAG TWO COLLECTION

PATIENT SAMPLE COLLECTION INSTRUCTIONS FOR THE FOLLOWING PROFILE(S)

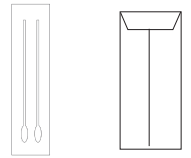
Metabolomix+*	Urine	#3200
Add-on Toxic Clearance Profile*	Urine	#3203
Add-on Comprehensive Urine Elements*	Urine	#3204
Add -on SNP - APO E (C112R + R158C)	Buccal Swab	#5204
Add -on SNP - MTHFR Combined (A1298C + C677T)	Buccal Swab	#5201
Add -on SNP - TNFA	Buccal Swab	#5203
Add -on SNP - COMT (V158M)	Buccal Swab	#5202

BAG TWO COLLECTION MATERIALS FOR SAMPLE

COLLECTION MATERIALS FOR URINE

Green-top Preservative Tube | Blue-top Amber Tube | Green-top Urine Tube | Blue-top Urine Tube | Plastic cup with Lid (2) | Pipette

FOR SALIVA



Cotton Swabs and Package | Envelope

REQUIRED MATERIALS

- Foam Insulator box
- Freezer brick
- Absorbent pad
- Test requisition form
- Biohazard bag
- Genova sample collection pack box
- FedEx® Clinical Lab Pak and Billable Stamp
- Collection labels (5)

IMPORTANT INFORMATION BEFORE YOU BEGIN THE URINE AND SALIVA COLLECTION

URINE COLLECTION

24 HOURS BEFORE THE TEST:

- **Eat usual diet,** but avoid over-consuming any single food or extreme diet
- **Fluid intakes** should be limited to eight (8) 8-ounce glasses of fluid over a 24 hour period

NIGHT BEFORE THE TEST:

- **You must fast** overnight prior to your urine/swab collection
- **Females** should not collect urine during a menstrual period
- **Freeze** the enclosed freezer brick overnight before shipping.
- Please note, patients **may not** be treated with provocation agent for purposes of testing.

Urine Tube Preservative

- **Avoid** contact with the skin and eyes. For eye contact, flush with water thoroughly for 15 minutes. For skin contact, wash thoroughly with soap and water. If ingested, contact poison control center immediately.

SALIVA COLLECTION (ONLY FOR GENOMICS ADD-ON TESTING)

NIGHT BEFORE THE TEST:

- **Use** your normal nightly routine of brushing and flossing of teeth, but **do not use mouthwash**

MORNING OF COLLECTION

- **Specimen must be collected immediately upon rising. Do not** practice normal oral hygiene routine, **do not eat or drink anything other than water.**
- Just prior to collection, **wash hands** completely with hand soap

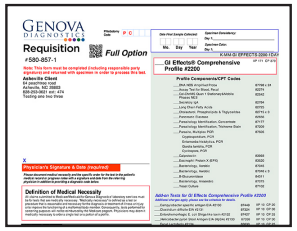
* Not available in New York

If any items are missing or expired, or liquid is spilled, call Client Services at 800.522.4762 and press "1"

URINE COLLECTION

1. **Label all tubes with the patient's date of birth. Do not discard tube fluid.**

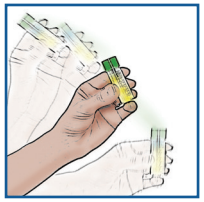
2. **Write patient's first and last name, date of birth, gender and date of collection** on the Test Requisition Form.


GENOVA DIAGNOSTICS
Requisition Full Option
#580-857-1
GI Effects® Comprehensive Profile #2200
Profile Components/CPT Codes
Definition of Medical Necessity

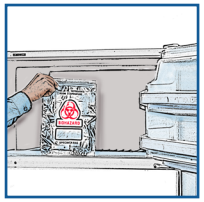
3. **If you wake up to urinate during the night** (within six hours of waking) **collect** that urine into one of the provided urine cups (3/4 full), place lid on cup then refrigerate. **Upon waking**, **collect** your urine into the second urine cup (3/4 full), and pass any additional urine into the toilet. **Mix** the two urine collections back and forth between the 2 cups to achieve a uniform mixture.

4. **Use** the pipette to transfer urine from the collection container into the Green-top Preservative Tube, Blue-top Urine Tube, Blue-top Amber Tube, and Green-top Urine Tube until all are nearly full.

5. **Recap** the tubes tightly and **shake**.

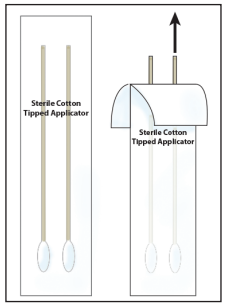


6. **Place** the tubes into the biohazard bag labeled BAG ONE and **freeze** for a **minimum of 2 hours**.



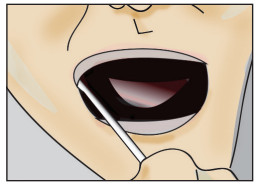
SALIVA COLLECTION (ONLY FOR GENOMICS ADD-ON TESTING)

1. **Keeping the packet intact, peel** open the package labeled, "Sterile Cotton Tipped Applicator."
Only peel back the package far enough to remove the cotton swab applicator.



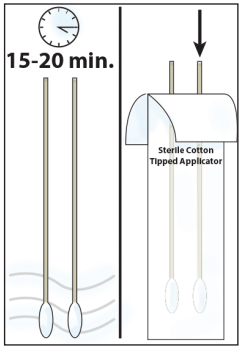
2. **Remove** one applicator.
Avoid contact with the cotton tip.

3. **Open** your mouth widely and insert applicator. For at least 30 seconds, **aggressively scrape** the inside of your cheek using a back and forth, and up and down motion. **Rotate** the applicator several times, and **swab** between the cheek and gums. Avoid excessive saliva.



***Note**: Follow these instructions carefully to ensure the swab collects a sufficient amount of cheek cells. If there is not enough DNA collected on the applicator, a recollection will be required.*

4. **REPEAT FIGURES 2 - 3 WITH SECOND SWAB**



5. **Allow** swabs to air dry for 15-20 minutes, then replace them (swab first) into the swab applicator package.

6. **Print** Full name, collection date, and date of birth on specimen collection label. **Place** the specimen collection label on the envelope.

7. **Insert** swab applicator package into the letter envelope and seal. Deliver the envelope, along with the frozen bag containing urine sample, to your healthcare provider's office.