

# Dr. Dimitris Tsoukalas MD, Ph.D.

#### For the clinician

Patient ID:	Date of Birth:
Sex:	Exam Date:

# **Results Report**

Metabolomic Analysis® is a test performed on the blood and urine for the quantitative analysis of a person's metabolites. Metabolites are very small molecules involved in the body's biochemical reactions, metabolism. The ability to carry out metabolic reactions depends on the adequacy of cofactors of the responsible enzymes (vitamins, minerals, trace elements, amino acids, fatty acids). The evaluation of the results is based on the absolute values of the metabolites, as well as their relations with other metabolites in all the metabolic pathways

The analysis accurately identifies deficiencies and metabolic disorders, which contribute to the onset of chronic and autoimmune diseases. Simultaneous analysis of >80 metabolites and 15 central metabolic pathways is performed to identify the factors that lead to the occurrence of disease. The advantage of the methology used is that it can detect marginal deficiencies and metabolic disruptions that is difficult to be identified with standard quantification techniques.

Metabolomic Analysis® is divided to three categories: Organic Acids, Fatty Acids, Serum Metabolites.

## **ORGANIC ACIDS**

Organic acids are intermediates in the chemical reactions that take place in the human body. They are produced in the energy production and detoxification pathways, during the metabolism of neurotransmitters, in the metabolism of proteins, carbohydrates, fatty acids or from the microbial flora.

# 1. Energy production (Krebs Cycle)

Percentage difference of more than 20%, between citric acid and aconitic acid

Oxidation of the enzyme aconitase, excess iron (hemochromatosis), iron deficiency (anemia), toxicity of mitochondria by heavy metals, congenital polymorphism of aconitase.

Symptoms: Metabolic stress, weakness, hypertension, high rate of aging, Friedreich ataxia (in cases of genetic defects).

High Fumaric acid

Q10 deficiency, mitochondrial dysfunction. Elevation of succinic, fumaric and malic levels is possibly caused by the deficiency in Q10 or cytochrome C and insufficient use of NADH, the basic derivative of the citric acid cycle.

Symptoms: Metabolic stress, weakness, disturbance in the metabolism of carbohydrates and fatty acids, hyperinsulinemia, chronic degenerative diseases

# High 3-Hydroxy 3-methyl-glutaric

Precursor metabolite of cholesterol and Q10. Statin use, suppression of HMG-CoA reductase, mitochondrial dysfunction. Insulin activates and glucagon inhibits HMG-CoA reductase. Symptoms: Fatigue, weakness, fibromyalgia, myalgia, myopathy, chronic degenerative diseases, myoglobinaemia, may contribute to rhabdomyolysis

## 2. Carbohydrate Metabolism

# High 3-Hydroxybutyric acid

Ketone body, increases in cases of fasting, diet with reduced carbohydrate content, diabetes or disorder of glucose metabolism (metabolic syndrome), insufficient glucose uptake at the cellular level, deficiencies in cytochrome enzymes. Symptoms: May be asymptomatic, metabolic acidosis, excess fatigue on physical exercise.

#### 3. Oxidative stress

### High 2-Hydroxyisobutyric acid

Intermediate metabolite of GABA. Metabolite of chemical additives of gasoline. Low GABA levels due to B6 deficiency, chemical toxicity, alteration of the bacterial flora, disturbance of nitrogen management.

## High Pyroglutamic acid

Intermediate metabolite of the glutathione cycle. Increased oxidation, glutathione deficiency, lack of amino acids that are required for glutathione synthesis (glutamine, glycine, cysteine, methionine), paracetamol toxicity, mitochondrial dysfunction. Symptoms: Increased oxidation levels, increase demands of antioxidants, especially in chronic diseases where glutathione requirements are higher, high rate of aging due to oxidation.

## 4. Biomarkers of B complex vitamins

### High Methylsuccinic acid

Mitochondrial dysfunction due to B2 deficiency. Fatigue, symptoms associated with increased oxidation, decreased exercise tolerance

#### 5. Neurotransmitter metabolism

### High 2-Hydroxyisobutyric acid

Intermediate metabolite of GABA. Metabolite of chemical additives of gasoline. Possible causes: Low GABA levels due to B6 deficiency, chemical toxicity, alteration of the bacterial flora, disturbance of nitrogen management.

# High Vanillylmandelic acid

Metabolite of epinephrine (adrenaline). Elevated levels are due to increased adrenaline clearance due to sympathetic reaction to chronic stress. Symptoms: Sleep disorders, headache, hypertension, difficulty managing stress, bowel disorders and fatigue.

#### 6. Microbiome status

## High 4-Hydroxyphenylacetic acid

When elevated, it is associated with dysbiosis and growth of anaerobic bacteria. It can be associated with malabsorption of tyrosine due to low HCL production in the stomach and lactose intolerance. Use of antibiotics targeting primarily aerobic bacteria that promote the growth of protozoa and anaerobic bacteria and increase 4-Hydroxyphenylacetate levels. Consumption of highly processed foods and especially processed simple carbohydrates promotes dysbiosis. Symptoms are related to intestinal dysbiosis such as diarrhea, constipation, steatorrhea, abdominal distention (bloating), allergic reactions due to intestinal permeability, malabsorption and nutritional deficiencies, fibromyalgia, mood disorders, impaired immune defenses, Inflammatory diseases (autoimmune diseases, arthritis,eczemas, psoriasis, obesity, metabolic syndrome, autism, abdominal pain, irritable bowel syndrome, inflammatory bowel disease, celiac disease, gastro- esophageal reflux disease (GERD), gastroenteritis, diverticulitis, acne, chronic fatigue syndrome and recurrent infections).

# 8. Ketone & Fatty acids oxidation

High 2-Hydroxyisobutyric acid

Intermediate metabolite of GABA. Metabolite of chemical additives of gasoline. Low GABA levels due to B6 deficiency, chemical toxicity, alteration of the bacterial flora, disturbance of nitrogen management.

# High Methylsuccinic acid

Mitochondrial dysfunction due to B2 deficiency. Fatigue, symptoms associated with increased oxidation, decreased exercise tolerance

### High 3-Hydroxybutyric acid

Ketone body, increases in cases of fasting, diet with reduced carbohydrate content, diabetes or disorder of glucose metabolism (metabolic syndrome), insufficient glucose uptake at the cellular level, deficiencies in cytochrome enzymes. Symptoms: May be asymptomatic, metabolic acidosis, excess fatigue on physical exercise.

## High Adipic or Suberic acid

Possible causes: Insufficient fatty acid oxidation, deficiency of carnitine, exposure to environmental toxins that alter lipid metabolism, if only adipic is increased possible exogenous intake of gels or flavor enhancers. Symptoms: Periodic mild fatigue, mitochondrial dysfunction, nausea, vomiting, hypoglycemia, recurrent infections, "sweaty foot odor", lack of attention in children, metabolic acidosis.

## 9. Vitamin C, E, β-carotene

## High 3-Hydroxy 3-methyl-glutaric

Precursor metabolite of cholesterol and Q10. Statin use, suppression of HMG-CoA reductase, mitochondrial dysfunction. Insulin activates and glucagon inhibits HMG-CoA reductase. Symptoms: Fatigue, weakness, fibromyalgia, myalgia, myopathy, chronic degenerative diseases, myoglobinaemia, may contribute to rhabdomyolysis

### **FATTY ACIDS**

Fatty acids play a central role in health, especially those that are not synthesized in the body but are obtained through the diet, the essential fatty acids. They are structural components of the membrane of all cells, regulate the immune response, are involved in the production of steroid hormones and other cell mechanisms. The categories of fatty acids include Saturated, Omega-3 and Omega-6 and Monounsaturated fatty acids. Assessment of fatty acid levels allows the quantitative and qualitative assessment of fatty acid intake and their degradation in the presence of cofactors. Metabolomic Analysis analyzes fatty acids from all 4 fatty acid families in plasma, capturing the levels of total fatty acids as well as the ratio between them.

#### **POLYUNSATURATED OMEGA 3 FATTY ACIDS**

High α-Linolenic acid (C18:3 ω3)

Essential omega-3 fatty acid, a structural component of cell membranes, is involved in the synthesis of anti-inflammatory eicosanoid hormones. Converts to EPA and DHA on zinc adequacy. Found in cold pressed oils and nuts such as linseed oil, walnuts, hemp seed oil and chia seed oil. Possible causes: Increased intake from diet or supplementation.

Symptoms: Diarrhea, oily skin and hair, poor wound healing, gastrointestinal disorders, hormonal imbalance and oxidative stress.

#### POLYUNSATURATED OMEGA 6 FATTY ACIDS

High Dihomo-y-linolenic acid (C20:3ω6)

Precursor metabolite of arachidonic acid (AA). Substrate for the production of anti-inflammatory prostaglandins, which control the pro-inflammatory action of AA. It works in synergy with omega-3 fatty acids. Contained in bouranza oil and evening primrose oil. Possible causes: Increased intake due to LA or DGLA supplementation or consumption of foods high in seed oils. Increased levels of insulin promote the conversion of DGLA to AA. Low rates of conversion to AA and PGE1 due to lack of cofactors (vitamins B2, B3 and C, P-5-P, Zn and Mg). Symptoms: Insulin resistance, hyperinsulinemia, chronic inflammatory conditions especially when combined with insufficient omega-3 fatty acids.

### MONOUNSATURATED-POLYUNSATURATRED FATTY ACIDS

Low Nervonic acid (C24:1ω9)



Nervonic acid improves brain function and prevents demyelination. Found in breast milk, flaxseed, borage, salmon, yellow mustard. Possible causes: Inhibition of desaturation due to insulin deficiency, insulin resistance or increased glucagon secretion.

Symptoms: Demyelination, multiple sclerosis.

#### SATURATED FATTY ACIDS

High Palmitic acid (C16:0)

Priority use by the body during intense exercise. Nutritional sources: coconut oil, palm oil, milk fat. Possible causes: Diet high in simple carbohydrates and sugars, hyperinsulinemia, mitochondrial dysfunction, if palmitic and palmitic acid are particularly elevated possible hyperinsulinemia and hypercortisolemia. Symptoms: Hyperinsulinemia, hypercholesterolemia, mitochondrial dysfunction, chronic inflammatory diseases (atherosclerosis, cardiovascular disease, stroke, etc.).

#### **RATIOS**

High Arachidonic / EPA ratio

Proinflammatory status marker representing the balance between  $\omega 3$  and  $\omega 6$  for the regulation of eicosanoids in tissue functions.

Possible causes: Diet high in meat and eggs of corn-fed animals and increased intake of foods containing corn oil, hyperinsulinemia.

Symptoms: Dry skin with itching that worsens in the cold, chronic inflammatory diseases.



The specific tests concern chemical chain reactions (one reaction occurs after another) and mainly evaluate the relationship of one metabolite in relation to others and not the absolute values. Thus a value may appear normal or out of the normal range and be evaluated differently. The test results reflect the metabolic status and needs of the body to function better under current conditions. They should not be interpreted as 'good' or 'bad' but should be evaluated by the treating physician taking into account the patient's medical history.

The Metabolomic Analysis® test is performed in collaboration with one of the top 5 laboratories conducting these analyses, in Europe and the USA, and meets the high technical standards required to conduct tests certified by the National Institute of Standards and Technology (NIST), the European Research Network for the Diagnosis and Treatment of Inherited Metabolic Disorders (ERNDIM, the world-class scientific institute with the highest laboratory standards) and the US Centers for Disease Control (CDC).

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