

Introducing Organic Acids inc.

Environmental Pollutants Test

Presented by Dr. Chris D. Meletis, ND



Today's Presenter:

Dr. Chris D. Meletis, ND

Dr. Chris Meletis is an educator, international author and lecturer. His personal mission is “Changing America’s Health One Person at a Time.” Dr. Meletis has authored 16 books and over 200 national scientific articles in journals including Natural Health, Alternative and Complementary Therapies, Townsend Letter for Doctors and Patients, Life Extension and Natural Pharmacy.

Dr. Meletis served as Dean of Naturopathic Medicine and Chief Medical Officer for 7 years for the National College of Naturopathic Medicine (now the National University of Natural Medicine). He was awarded the 2003 Physician of the Year by the American Association of Naturopathic Physicians. He has a deep passion for helping the underprivileged and spearheaded the creation of 16 free natural medicine healthcare clinics in the Portland metropolitan area of Oregon.

Dr. Meletis serves as a consultant to US BioTek on the clinical application of its laboratory tests. The views expressed are his own.



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Organic Acid Review

- **Role in ATP Production**
- Considerations for Specific Dietary Nutrients
- **Fueling Mitochondria for Whole Body and Brain Performance**
- Neurotransmitters with Clinical Implications
- **Interventional Nutritional Supplementation**

Conditions Associated with Mitochondrial Dysfunction

- ★ • Alzheimer's Disease
- ★ • Anxiety
 - Bipolar disorder
 - Cancer
- ★ • Cardiovascular disease/Atherosclerosis
 - CFIDS
- ★ • Diabetes
 - Exercise intolerance
- ★ • Fatigue
 - Fibromyalgia
 - Huntington's disease
 - Myofascial pain
 - NAFLD
- ★ • Parkinson's disease
 - Sarcopenia
 - Schizophrenia
- ★ • Senescence/Aging



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Possible Mitochondria Dysfunctions – In Clinical Practice

Organ System	Possible symptom, disease or contributing factor
Brain	Developmental delay, mental retardation, autism, dementia, seizures, neuropsychiatric disturbances, atypical cerebral palsy, atypical migraines, stroke, and stroke like events.
Ears	Sensorineural hearing loss, aminoglycoside sensitivity
Eyes	Optic neuropathy and retinitis pigmentosa
Heart	Cardiac conduction defects (heart blockages), cardiomyopathy
Kidneys	Proximal renal tubular dysfunction (Fanconi Syndrome); possible loss of amino acids, magnesium, phosphorus, calcium and other electrolytes.
Liver	Hypoglycemia, gluconeogenic defects, nonalcoholic liver failure
Muscles	Hypotonia, weakness, cramping, muscle pain, ptosis, ophthalmoplegia
Nerves	Neuropathic pain and weakness (possibly intermittently), acute and chronic inflammatory demyelinating polyneuropathy, absent deep tendon reflexes, neuropathic gastrointestinal problems, fainting, absent or excessive sweating, aberrant temperature regulation
Pancreas	Diabetes and exocrine pancreatic failure
Systemic	Failure to gain weight, short stature, fatigue, respiratory problems including intermittent air hunger

*adapted from Molecular Nutrition & Food Research 2008, 52, 780-788

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Medications Linked to Mitochondrial Dysfunction

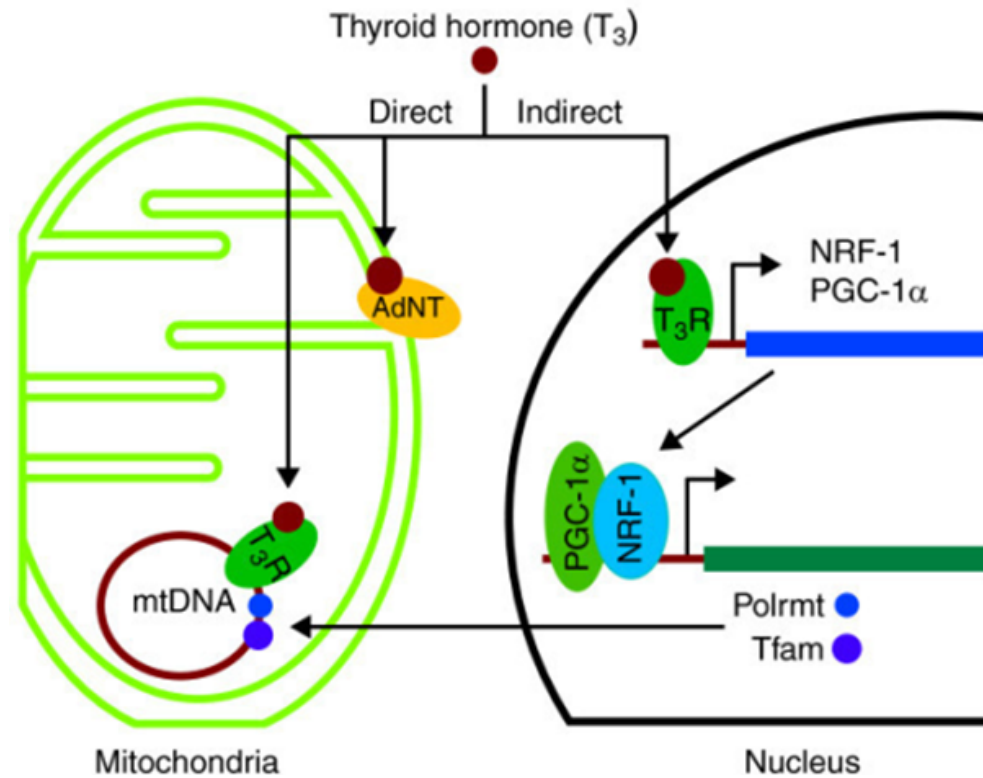
Drug Class	Medications
Alcoholism medications	Disulfiram (Antabuse)
Analgesic and anti-inflammatory	Aspirin, acetaminophen (Tylenol), diclofenac, fenoprofen, indomethacin, naproxen
Anesthetics	Bupivacaine, lidocaine, propofol
Angina medications	Perhexiline, amiodarone
Antiarrhythmic	Amiodarone
Antibiotics	Tetracycline, antimycin A
Antidepressants	Amitriptyline, amoxapine, citalopram, fluoxetine
Antipsychotics	Chlorpromazine, fluphenazine, haloperidol, risperidone, quetiapine, clozapine, olanzapine
Anxiety medications	Alprazolam (Xanax), diazepam (valium)
Barbiturates	Amobarbital, aprobarbital, butabarbital, butalbital, methylphenobarbital, pentobarbital, phenobarbital, primidone, secobarbital, thiobarbital
Cholesterol medications	Statins – atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin. Bile acids – cholestyramine, clofibrate, ciprofibrate, colestipol, colessevelam
Chemotherapy medications	Mitomycin C, proflomycin, adriamycin (also called doxorubicin and hydroxydaunorubicin and included in the following chemotherapeutic regimens – ABVD, CHOP, and FAC)
Dementia	Tacrine (Cognex), Galantamine (Reminyl)
Diabetes medications	Metformin (Glucophage), troglitazone, rosiglitazone, buformin
HIV/AIDS medications	Retrovir (AZT, ZDV, zidovudine) and several other medications
Epilepsy/Seizure medications	Valproic acid (Depacon, Depakene, Depakene syrup, Depakote, depakote ER, depakote sprinkle, divalproex sodium)
Mood stabilizers	Lithium
Parkinson's disease medications	Tolcapone (Tasmar, Entacapone (COMTan, also in the combination drug Stalevo)

*adapted from Molecular Nutrition & Food Research 2008, 52, 780-788

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The thyroid hormone T₃ is a primary regulator of mammalian mitochondrial biogenesis and can influence mitochondrial function both indirectly and directly.

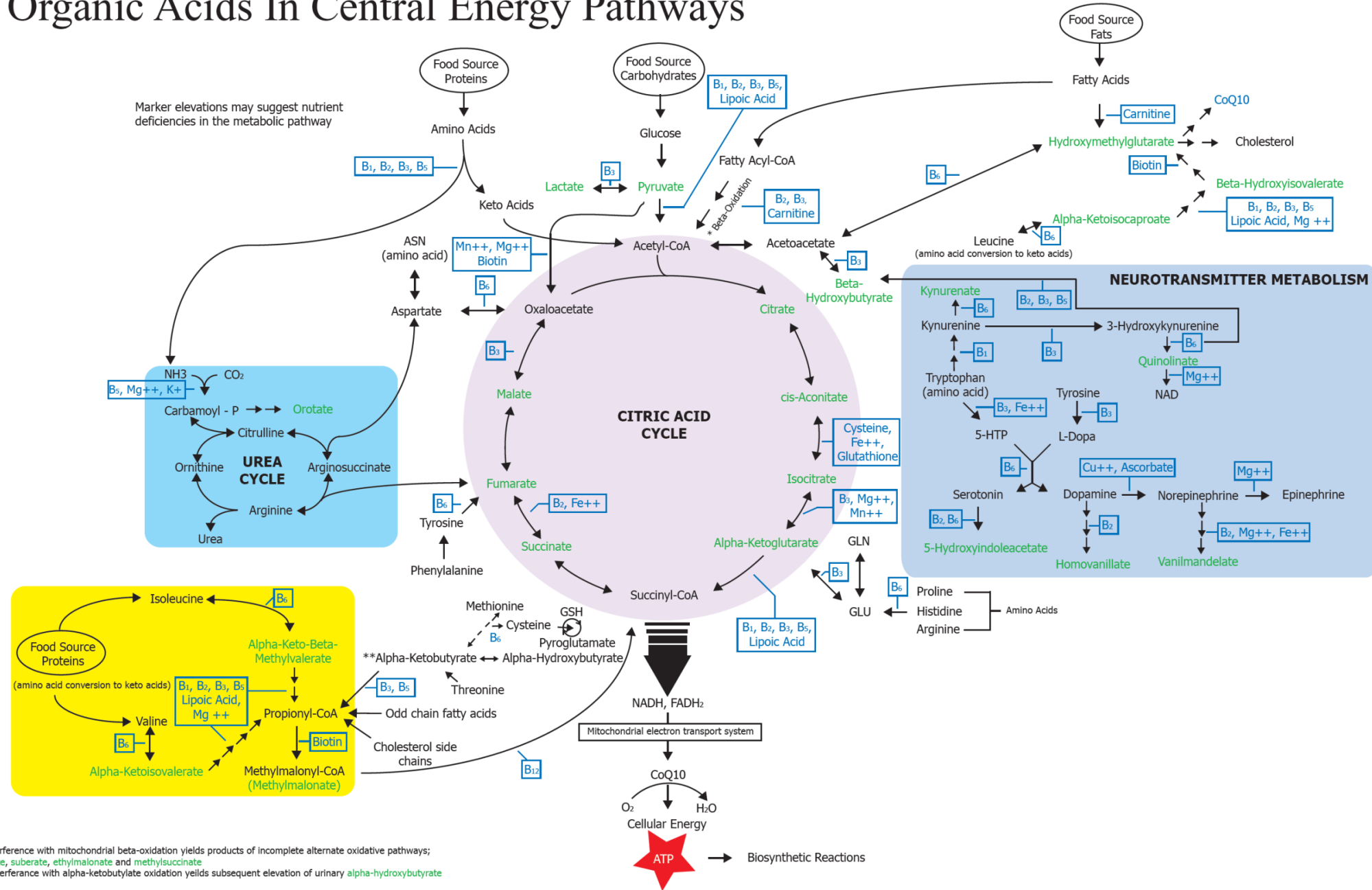
Leigh-Brown S, Enriquez JA, Odom DT - Genome Biol. (2010)

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Organic Acids In Central Energy Pathways



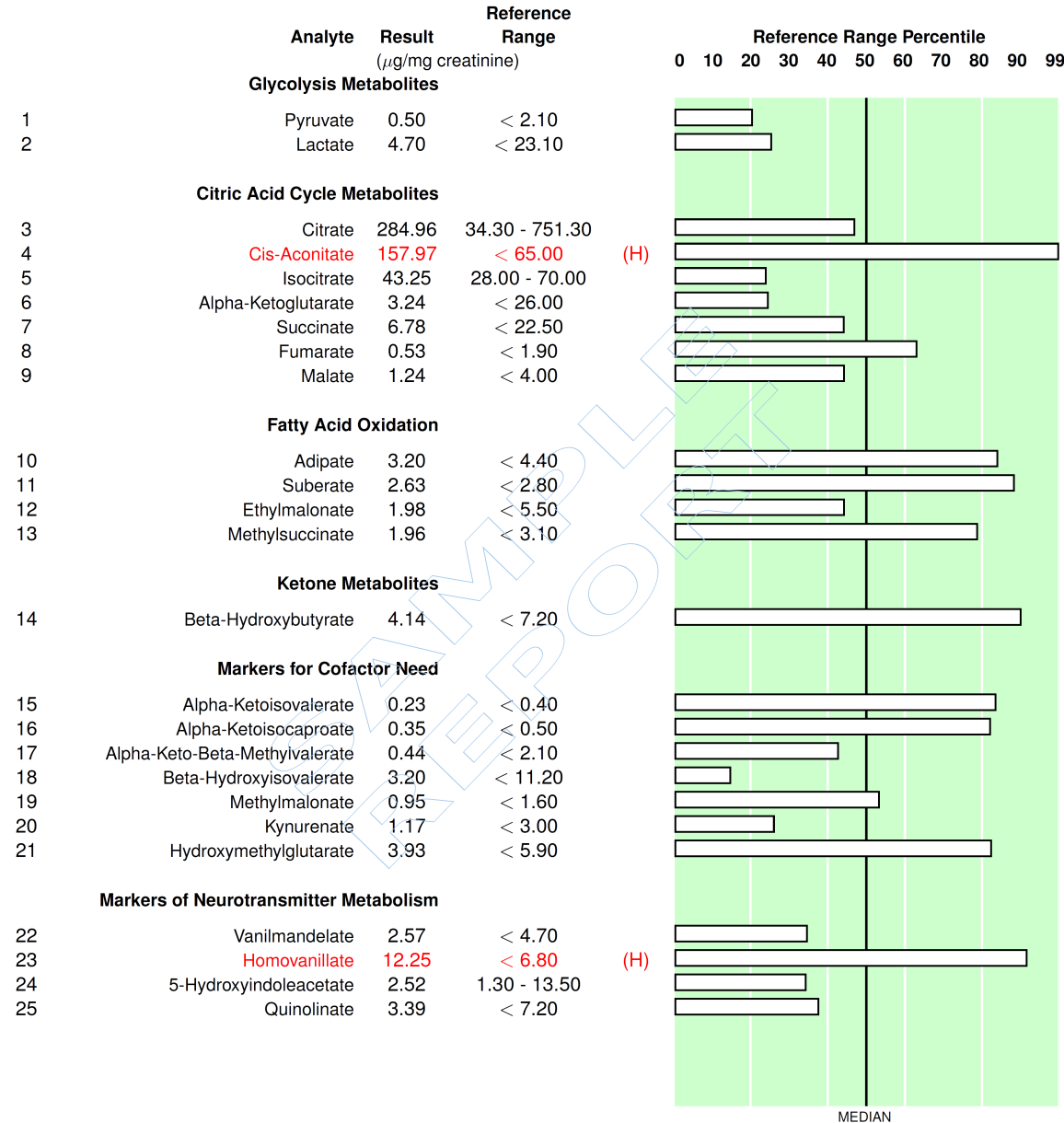
* Interference with mitochondrial beta-oxidation yields products of incomplete alternate oxidative pathways; adipate, suberate, ethylmalonate and methylsuccinate
 ** Interference with alpha-ketobutyrate oxidation yields subsequent elevation of urinary alpha-hydroxybutyrate



Physician:
Patient:
Accession:

Sex:
Age: 73
Sample Type: Dried Urine

Collected:
Received:
Completed:

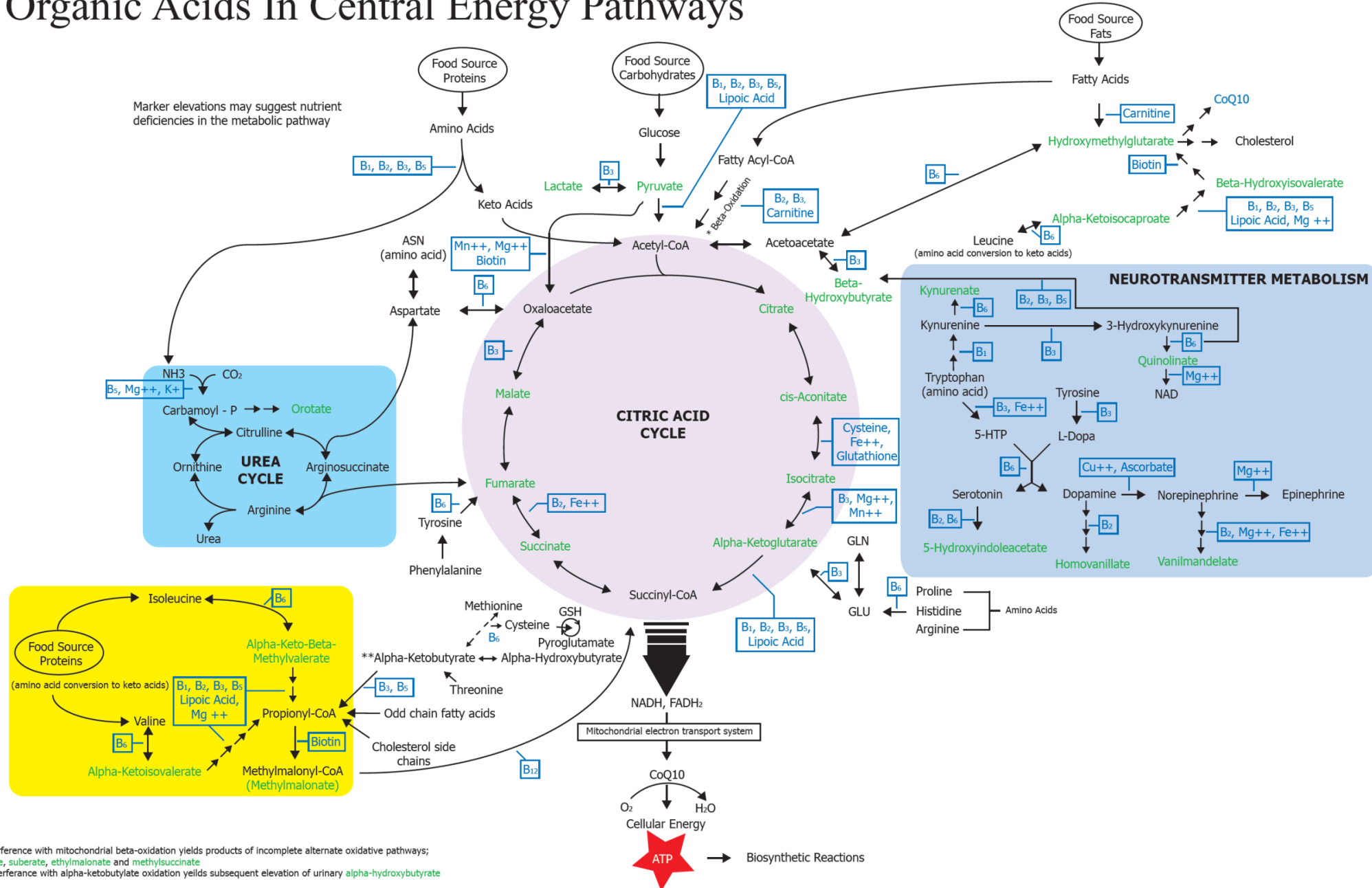


Testing Via
**Liquid Chromatography/
Triple Quadrupole Mass Spectrometry
(LC-MS/MS)**

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Organic Acids In Central Energy Pathways



* Interference with mitochondrial beta-oxidation yields products of incomplete alternate oxidative pathways; adipate, suberate, ethylmalonate and methylsuccinate
 ** Interference with alpha-ketobutyrate oxidation yields subsequent elevation of urinary alpha-hydroxybutyrate

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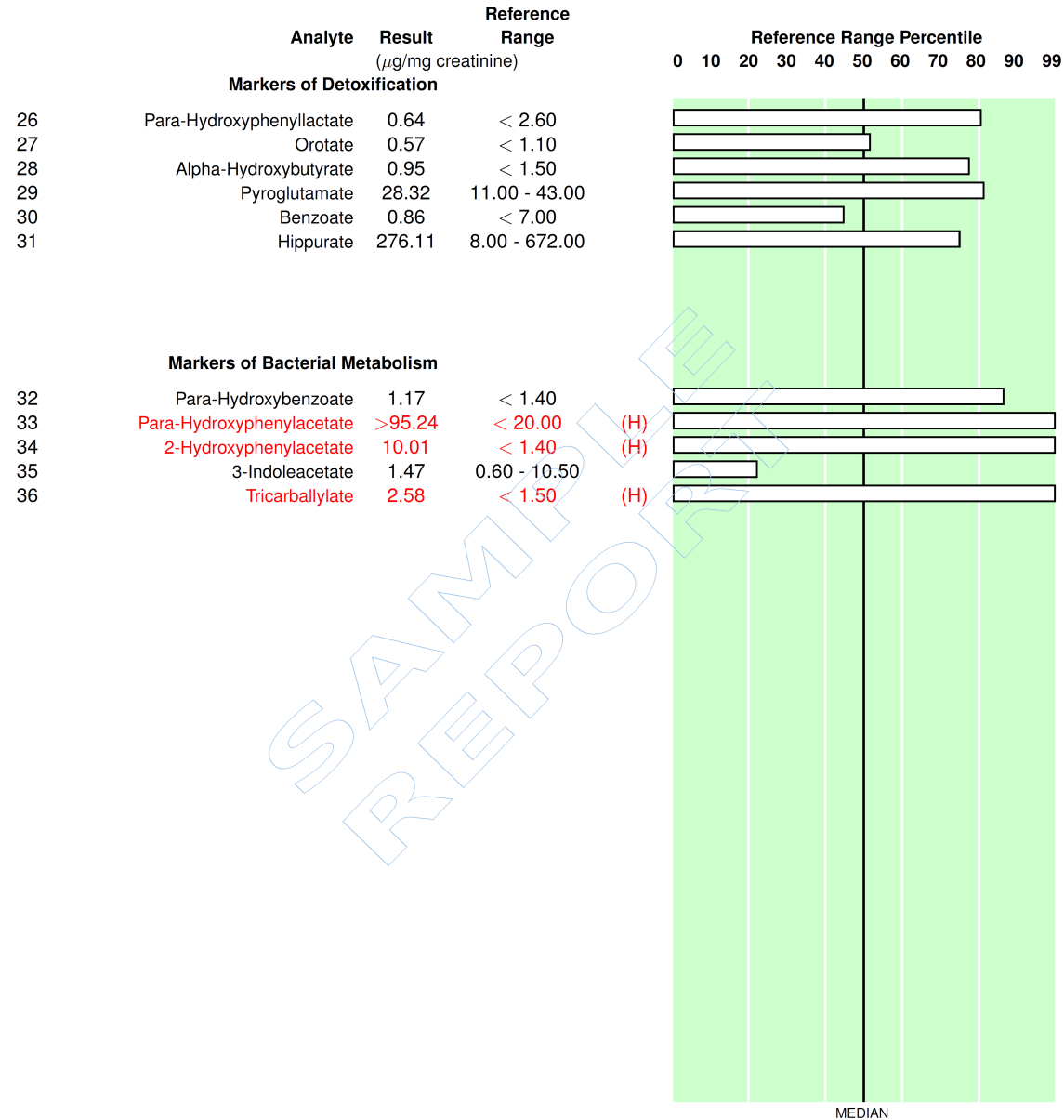
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Physician:
Patient:
Accession:

Sex:
Age: 73
Sample Type: Dried Urine
Collected:
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Completed:



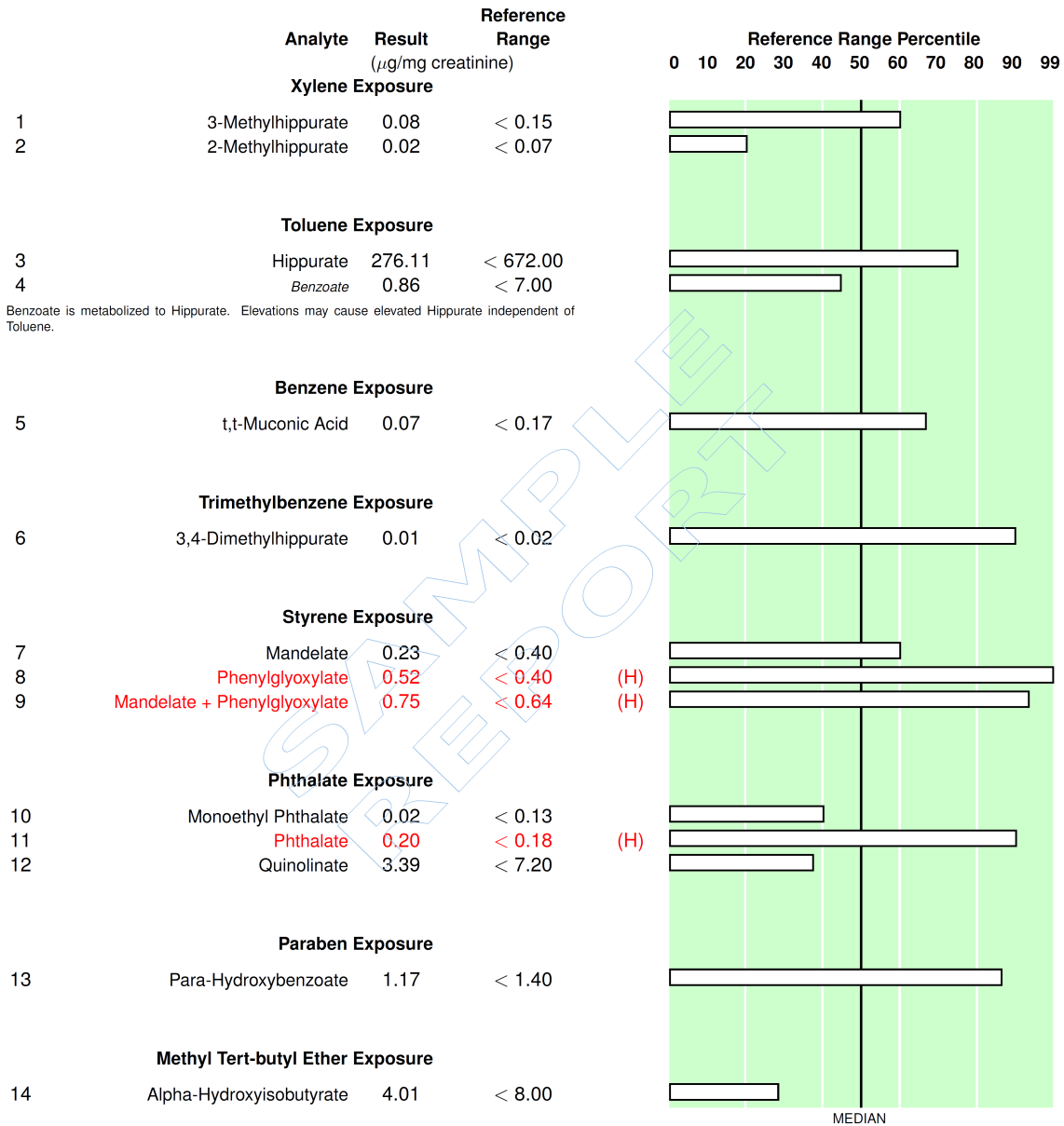
SAMPLE REPORT



Physician:
Patient:
Accession:

Sex:
Age: 73
Sample Type: Dried Urine

Collected:
Received:
Completed:



(Add-on Test to Organic Acid Test)

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Comprehensive Urinary Metabolic Profile

BTL001

Read all instructions carefully before beginning

Important information

- Samples must only be collected and shipped Monday, Tuesday or Wednesday.
- The sample must be shipped within 24 hours of collection.

Patient preparation

- Do not collect the sample during menstruation.
- Do not collect the sample during a urinary tract infection.

Procedures, medications and supplements

Invivo do not recommend any changes to prescribed or regular medications / supplements without seeking advice from a suitably qualified medical professional. However, some medications / supplements are known to have an impact on the test results. Please consult your healthcare provider or contact Invivo to discuss any regular medications or supplements.

Restrictive preparation diet

- 48 hours prior to collection, do not consume the following foods:

Beverages:

1. Tea
2. Coffee
3. Alcoholic drinks
4. Juice from the list of fruits or vegetables below

Fruits & vegetables:

1. Avocado
2. Tomato
3. Kiwi
4. Banana
5. Grapes / raisins
6. Pineapple
7. Plums / prunes
8. Plantain

Seeds & nuts:

1. Walnuts
2. Pecans

Other:

1. Ketchup
2. Jelly
3. Vanilla extract
4. Aged and processed cheeses

Preservatives within foods:

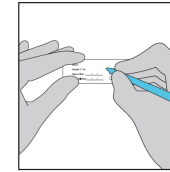
1. Sorbic Acid/Sorbate (preservative E200-203)
2. Benzoic Acid/Sodium Benzoate (preservative E 210-213)

- 12 hours prior to collection, avoid excessive water intake.
- On the morning of collection, do not consume food or drink until you have completed the test.

Kit contents

- 1 test requisition form
- 1 urine collection strip
- 1 urine collection cup
- 1 paper envelope
- 1 unpaid addressed grey mailing bag

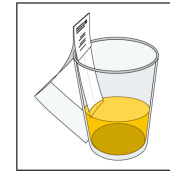
Sample collection



1. Clearly write the following details onto the urine collection strip and the test requisition form:

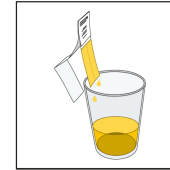
* Take care not to touch the absorbent pad.*

- Full name
- Date of birth
- Gender
- Collection date



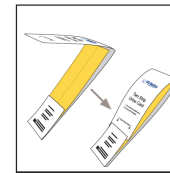
2. Collect urine into the urine collection beaker. Only collect the mid-stream of first morning urine before consuming any food or drink. Do not collect the first portion or urine.

3. Taking care not to touch the absorbent pad, place the absorbent pad into the urine sample. Leave the pad touching the urine sample until fully saturated, or for a minimum of 15 seconds.



4. Remove the absorbent pad from the sample and allow the excess sample to drip freely into the sample collection cup.

5. The sample must be left to **completely dry** before shipping. The sample can be air-dried for a minimum of 12 hours; however, humidity and temperature may prolong the drying time. Alternatively, you can use a hair dryer. The dryer must be set to a low temperature setting and held at least 3 inches away from the sample. The sample must not get hot.



6. Once completely dried, place the protective cover over the absorbent portion of the urine strip and tuck securely.

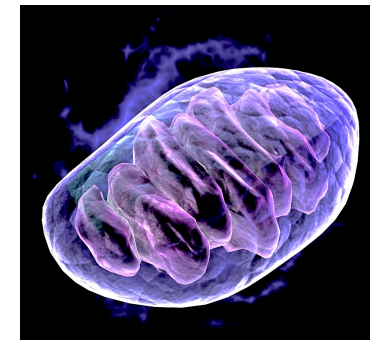
7. Place the dried and labelled strip into the paper envelope and seal tightly.

8. Place the paper envelope and completed test requisition form into the test kit box.

9. Place the test kit box into the unpaid addressed grey mailing bag and organise sample shipping.

Oxidative Damage, Aging and Mitochondrial Fate

- Mitochondria are responsible for 90-95% of free radicals in our cells, thereby disrupting healthy cells.*
- Mitochondria are exposed to 10x more free radicals than the rest of the cell.
- **By age 30, energy production drops by up to 10% per decade.**
- With decreased energy production, cellular function can become impacted leading to signs and symptoms of aging.

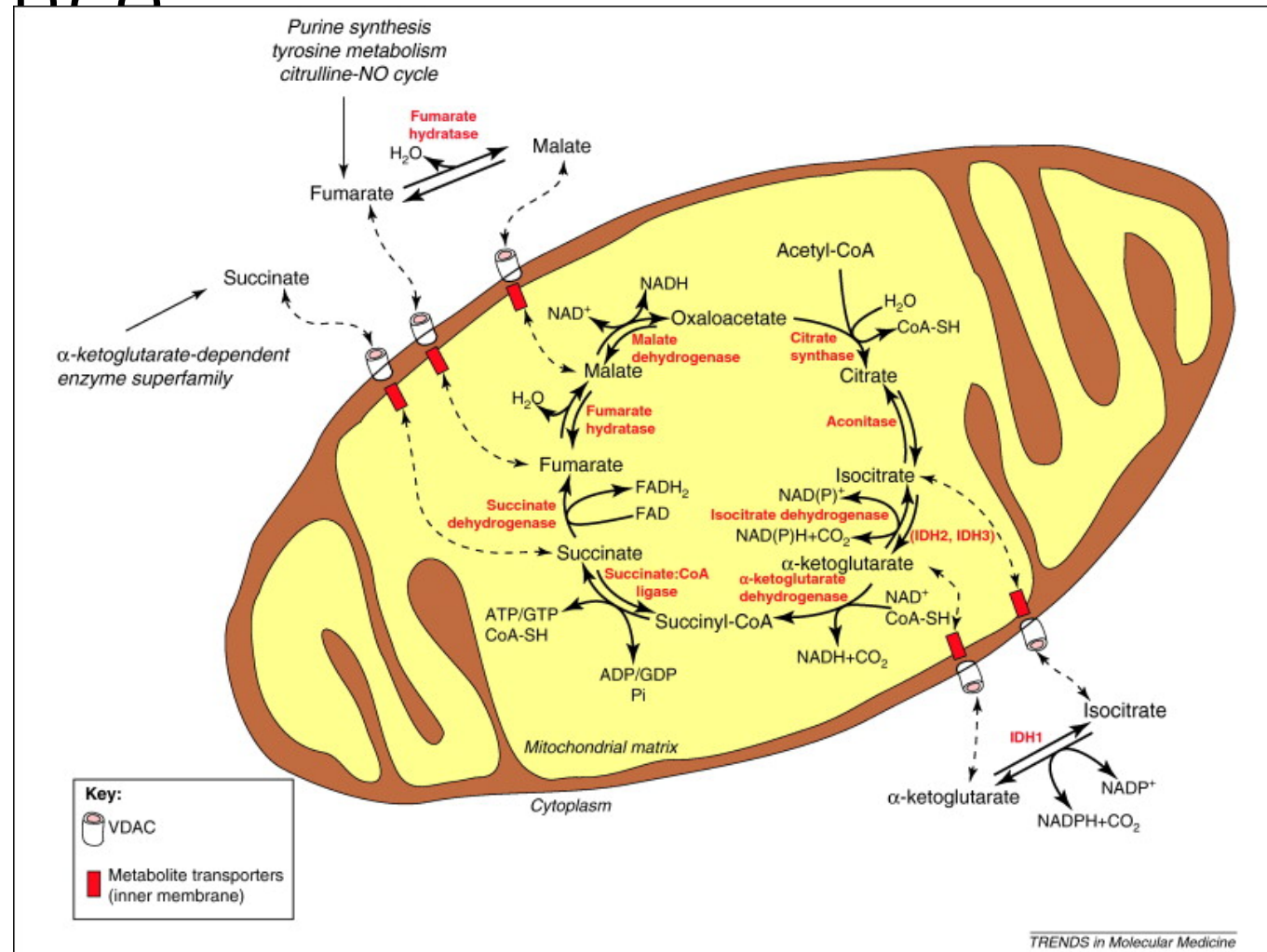


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Subcell Biochem. 2018;87:167-227.

Quantifying Inner Matrix of Mitochondria Performance



Trends Mol Med. 2011 Nov;17(11):641-9.

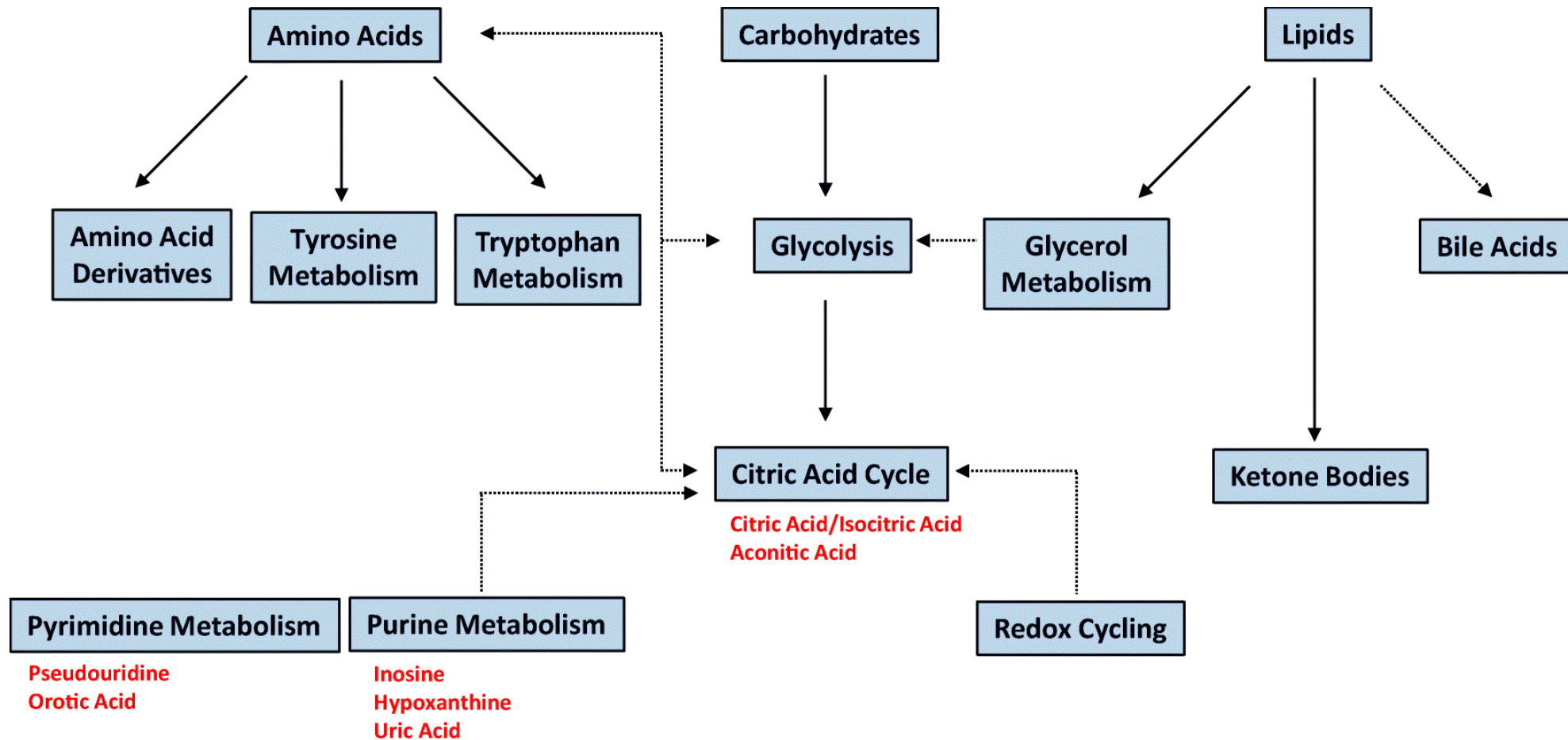
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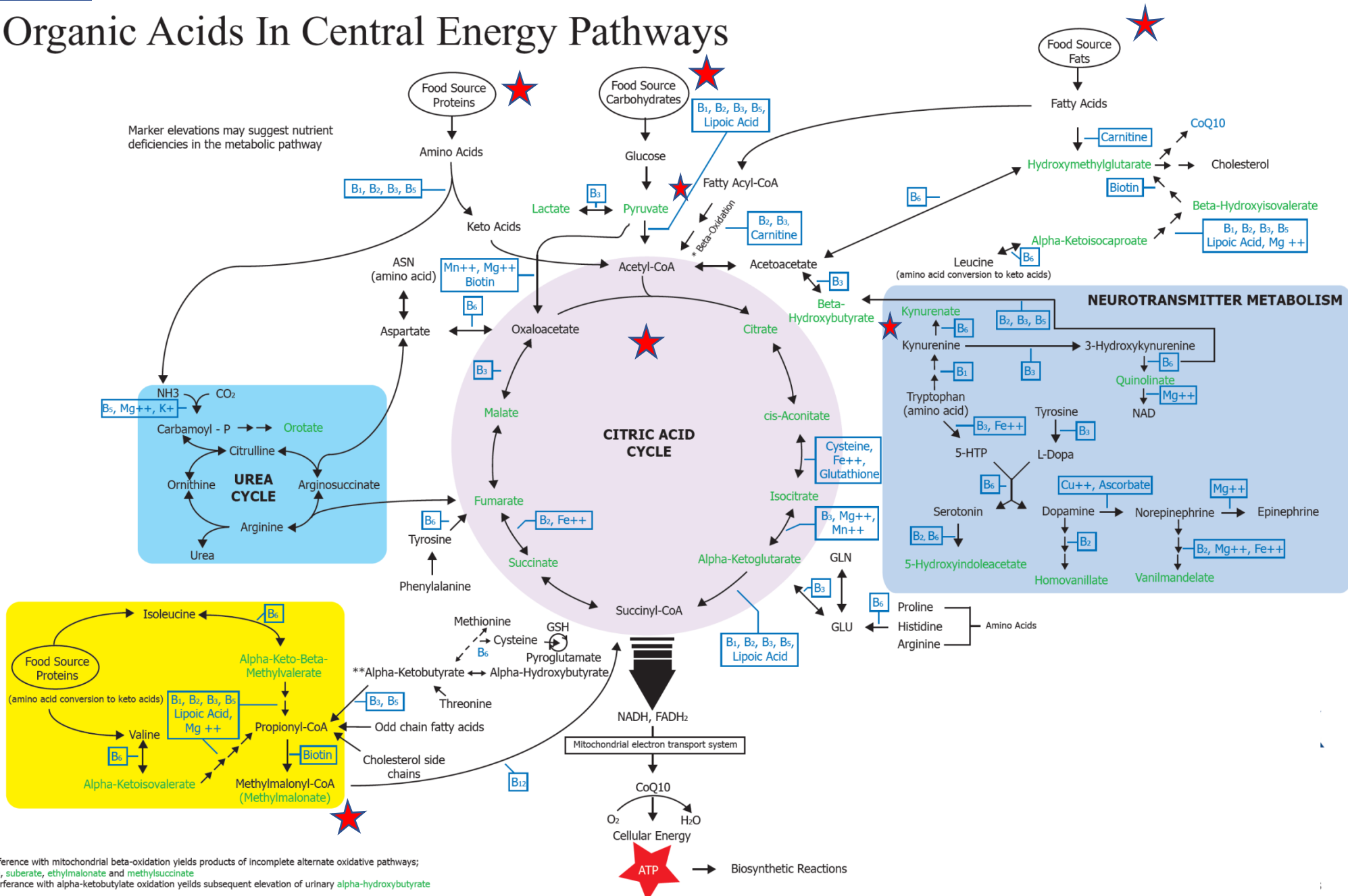
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Food as Fuel



Organic Acids In Central Energy Pathways



* Interference with mitochondrial beta-oxidation yields products of incomplete alternate oxidative pathways; adipate, suberate, ethylmalonate and methylsuccinate
 ** Interference with alpha-ketobutyrate oxidation yields subsequent elevation of urinary alpha-hydroxybutyrate



Sample Organic Acids & Environmental Pollutant Panels





Physician:
Patient:
Accession:

Sex:
Age: 73
Sample Type: Dried Urine

Collected:
Received:
Completed:

Analyte Result Reference Range (µg/mg creatinine)

Reference Range Percentile 0 10 20 30 40 50 60 70 80 90 99

Glycolysis Metabolites

Table with 3 columns: Analyte, Result, Reference Range. Rows: 1 Pyruvate 0.50 < 2.10, 2 Lactate 4.70 < 23.10

Citric Acid Cycle Metabolites

Table with 3 columns: Analyte, Result, Reference Range. Rows: 3 Citrate 284.96 34.30 - 751.30, 4 Cis-Aconitate 157.97 < 65.00 (H), 5 Isocitrate 43.25 28.00 - 70.00, 6 Alpha-Ketoglutarate 3.24 < 26.00, 7 Succinate 6.78 < 22.50, 8 Fumarate 0.53 < 1.90, 9 Malate 1.24 < 4.00

Fatty Acid Oxidation

Table with 3 columns: Analyte, Result, Reference Range. Rows: 10 Adipate 3.20 < 4.40, 11 Suberate 2.63 < 2.80, 12 Ethylmalonate 1.98 < 5.50, 13 Methylsuccinate 1.96 < 3.10

Ketone Metabolites

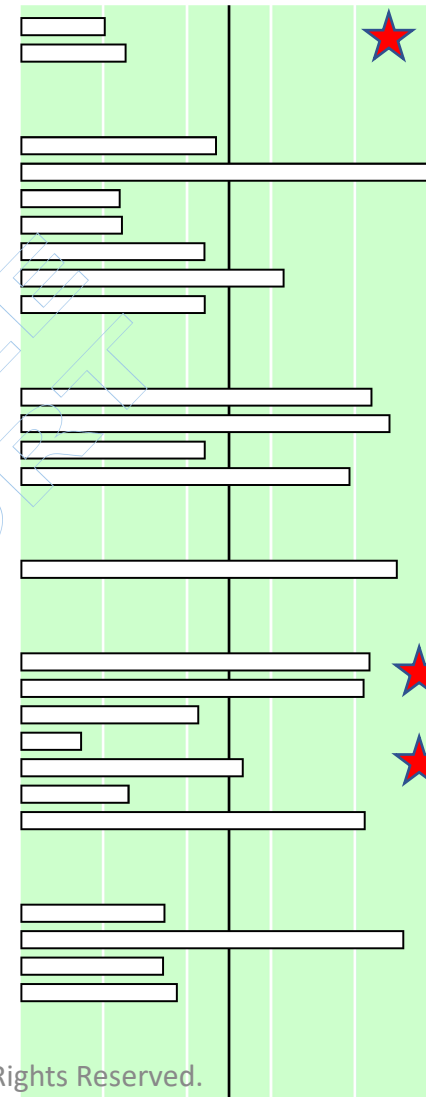
Table with 3 columns: Analyte, Result, Reference Range. Row: 14 Beta-Hydroxybutyrate 4.14 < 7.20

Markers for Cofactor Need

Table with 3 columns: Analyte, Result, Reference Range. Rows: 15 Alpha-Ketoisovalerate 0.23 < 0.40, 16 Alpha-Ketoisocaproate 0.35 < 0.50, 17 Alpha-Keto-Beta-Methylvalerate 0.44 < 2.10, 18 Beta-Hydroxyisovalerate 3.20 < 11.20, 19 Methylmalonate 0.95 < 1.60, 20 Kynurenate 1.17 < 3.00, 21 Hydroxymethylglutarate 3.93 < 5.90

Markers of Neurotransmitter Metabolism

Table with 3 columns: Analyte, Result, Reference Range. Rows: 22 Vanilmandelate 2.57 < 4.70, 23 Homovanillate 12.25 < 6.80 (H), 24 5-Hydroxyindoleacetate 2.52 1.30 - 13.50, 25 Quinolinat 3.39 < 7.20



Carbohydrate Metabolism +

Fatty Acid Metabolism

B12 Status

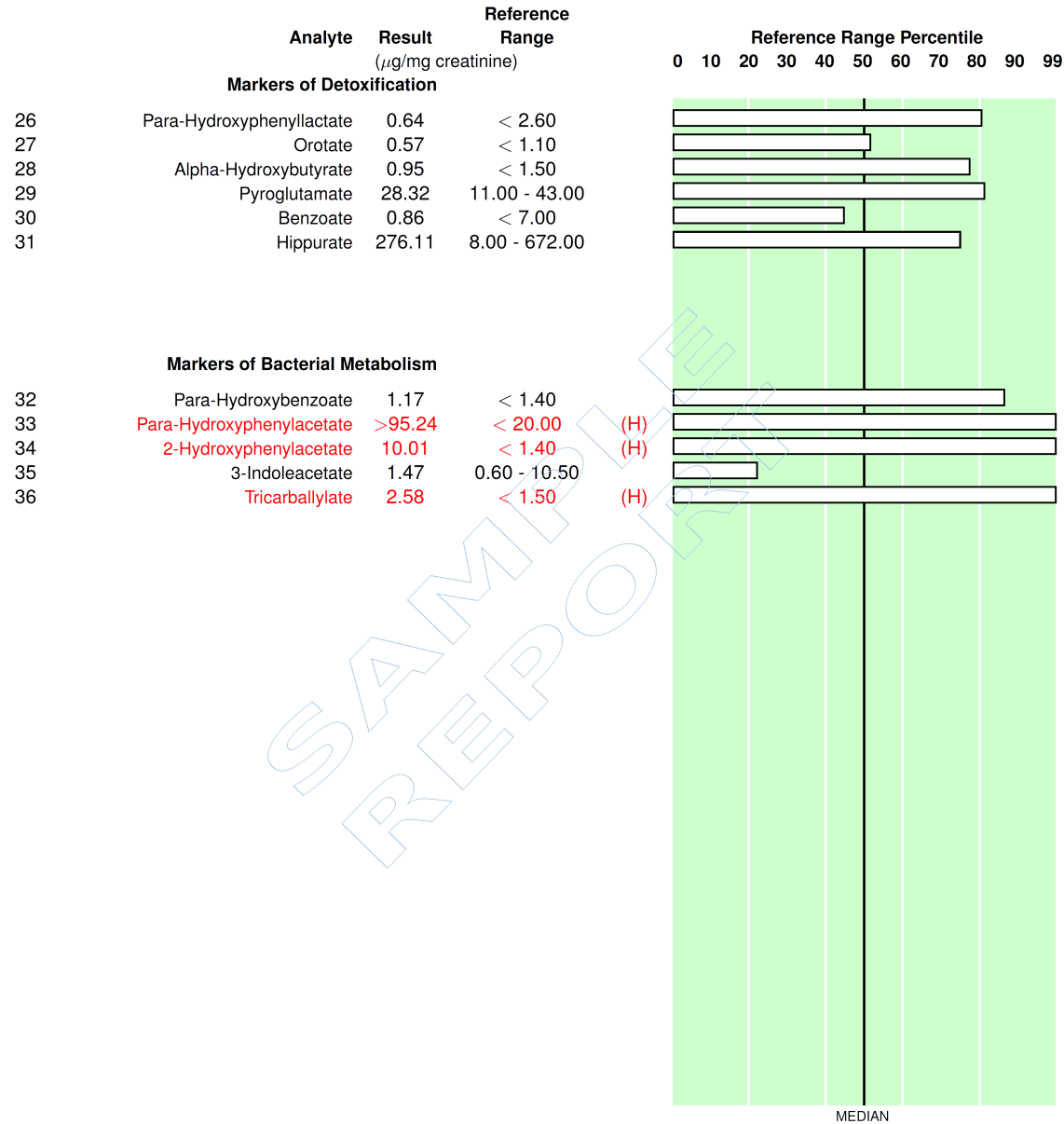
Citric Acid Cycle Metabolites





Physician:
Patient:
Accession:

Sex:
Age: 73
Sample Type: Dried Urine
Collected:
Received:
Completed:



SAMPLE REPORT

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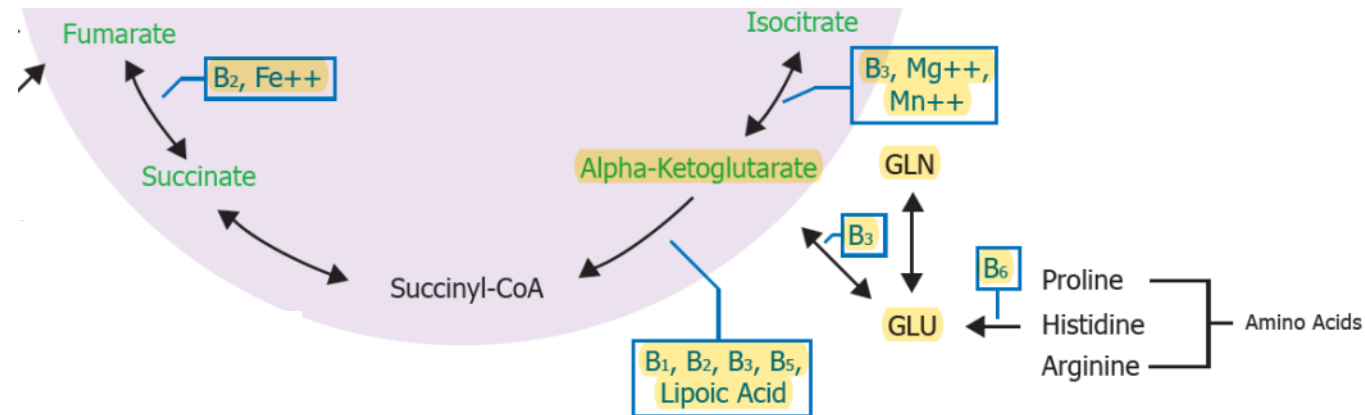


Importance of the Testing Citric Acid Cycle

- Impairments in the citric acid cycle can affect mitochondrial function and thus can have wide-reaching effects on health.
- Example, since citrate is involved in many metabolic and cellular processes, its metabolism through the citric acid cycle and electron transport chain may be important to the immune response.

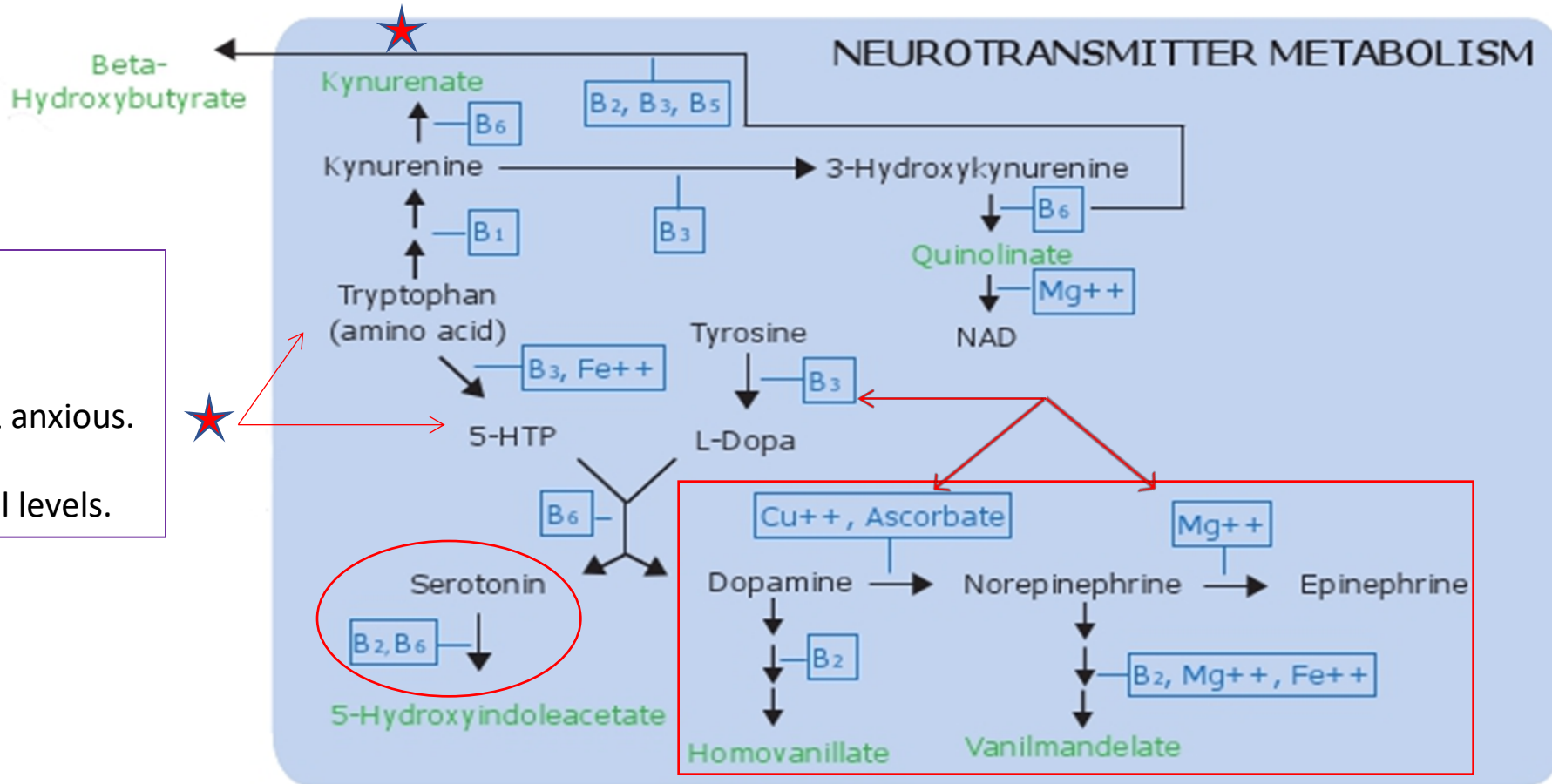
Glutamatergic, GABAergic and Neurotransmitters

Glutamate (Glu) and Gamma-aminobutyric acid (GABA) are the most abundant neurotransmitters in the cerebral cortex for the excitatory and inhibitory neurotransmission in the mature central nervous system. **Perturbation of these pathways are associated with several neurological and psychiatric disorders.**



Neurochemistry and Neuroinflammatory Trends

Adrenal Medulla
 50 y.o. male stress,
 "wired and tired" & anxious.
 Low normal Cortisol levels.



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Clinician to Clinician Discussion

Therapeutic Considerations





Symptoms & Nutrient Considerations Associated with Impaired Citric Acid Cycle

- Imbalanced levels of key players in the citric acid cycle are associated with specific symptoms and nutrient deficiencies.
- For example, high lactate is associated with muscle cramping, brain fog, and fatigue.
- Elevated lactate is also associated with **deficiencies of CoQ10, a nutrient critical to mitochondrial function, as well as B vitamins including biotin and lipoic acid.**

www.functionalmedicine.net/pdf/Insider%27s%20Guide_37.pdf Accessed April 22, 2019

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Epigenetics, Mitochondria, and the Citric Acid Cycle

- Epigenetics is also involved in the relationship between mitochondrial health and the citric acid cycle.
- Epigenetics are changes to DNA that do not alter the DNA sequence and yet affect gene activity.
- These epigenetic alterations act like switches that can turn genes on or off.
- Epigenetic changes can be passed on to both children and grandchildren and are triggered by such factors as lifestyle and toxin exposure.

<https://ghr.nlm.nih.gov/primer/howgeneswork/epigenome> Accessed April 19, 2019

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Epigenetic Reprogramming

- There is also a relationship between citrate metabolism, carbohydrate metabolism, fatty acid metabolism, and epigenetic reprogramming.
- Citrate plays a critical role in many pivotal cellular pathways and is a link between carbohydrate, fatty acid metabolism and protein modification.
- Through the citric acid cycle, citrate generates acetyl-CoA, which is a substrate for histone acetylation.
- This feature of citrate plays a critical part in the regulation of immune cell function.

Front Immunol. 2018 Feb 5;9:141.

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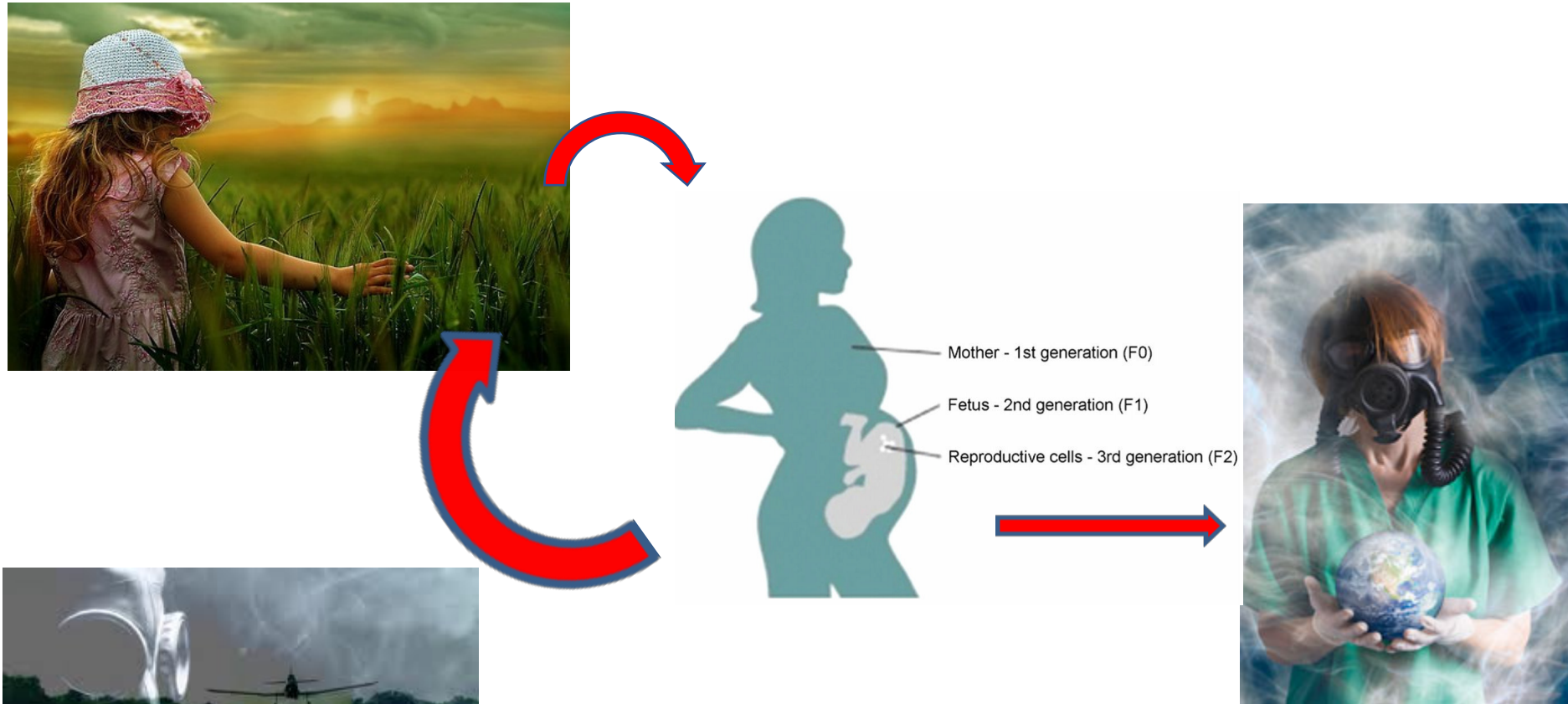
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Disease Potential Passed to the Future

Epigenetic changes occur within parents and grandparents can be passed to children.



European Journal of Human Genetics (2002) 10, 669-67
Discover Tuesday, June 11, 2013

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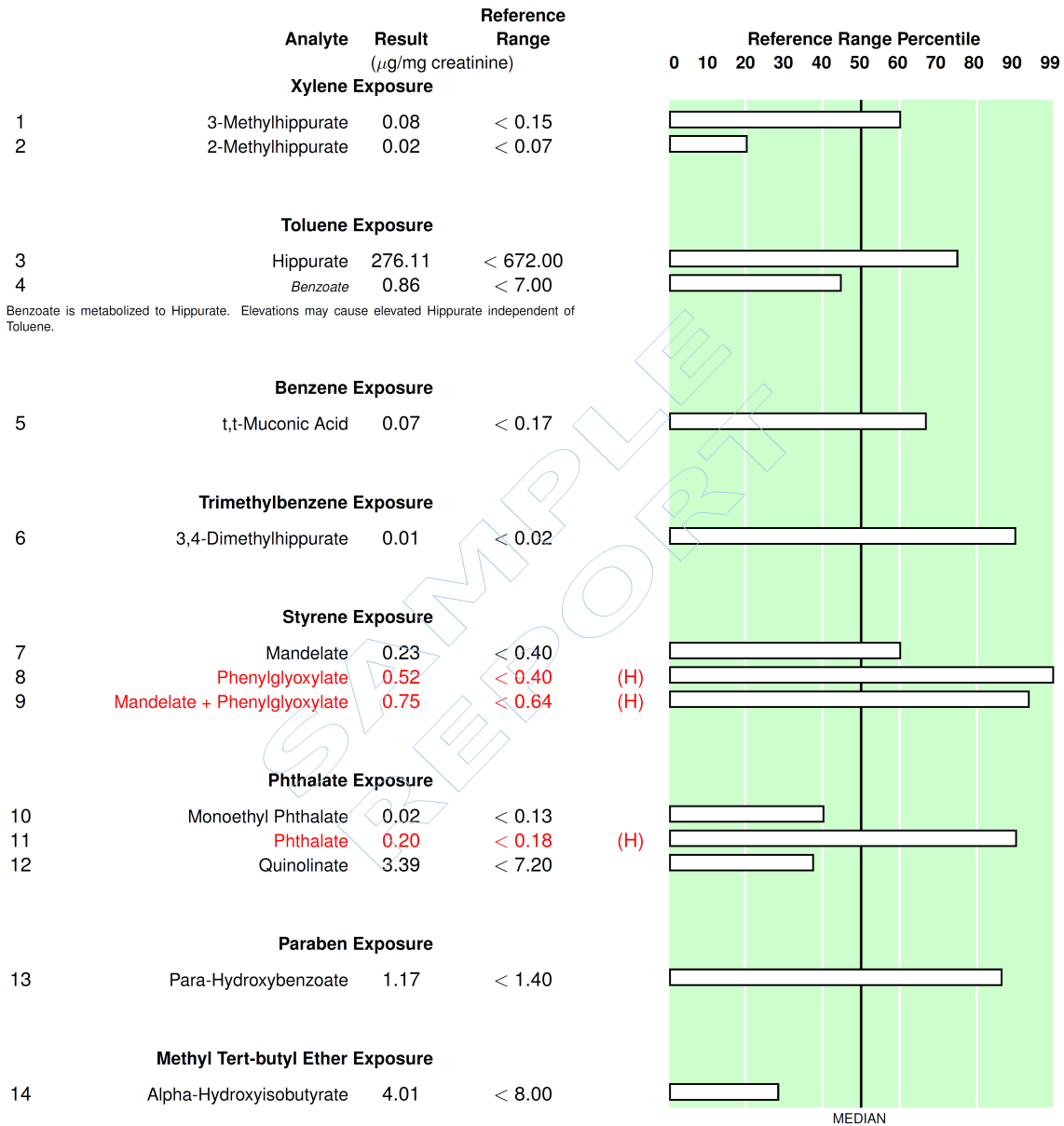
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Physician:
Patient:
Accession:

Sex:
Age: 73
Sample Type: Dried Urine

Collected:
Received:
Completed:



(Add-on Test to Organic Acid Test)

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Sources Environmental Toxins

Toxin	Possible Sources of Exposure
Phthalates	Wall coverings, tablecloths, floor tiles, furniture upholstery, shower curtains, garden hoses, swimming pool liners, rainwear, baby pants, dolls, some toys, shoes, automobile upholstery and tops, food packaging, sheathing for wire and cable, medical tubing, blood storage bags, carpets, paints, glue, insect repellents, hair spray, nail polish, rocket fuel, carpet back coating, floor tile, adhesives, cosmetics, pesticides, toothbrushes, automobile parts, tools, toys, and aspirin.
Benzene	Pesticides, wildfire smoke, plastics, resins, synthetic fibers, rubber lubricants, dyes, detergents, drugs, vehicle exhaust, ground water.
Toluene	Paint thinners, paintbrush cleaners, nail polish, glues, inks, stain removers, vehicle exhaust, cigarette smoke, and groundwater.
Parabens	Personal care products such as soap, shampoo, cosmetics, and perfume.
Styrene	Cigarette smoke, packaging, household, and building products, vehicle exhaust, emissions from copy machines.

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Phase I, II & III Detoxification

**Fat-Soluble
Toxins**

**Water-Soluble
Waste**

Phase I

Required Nutrients
-B Vitamins (B2,B3,B6 & B12)
-Folate
-Glutathione
-Antioxidants/Flavonoids
-[eg. Milk Thistle]
-Carotenoids
-Vitamin C
-Vitamin E

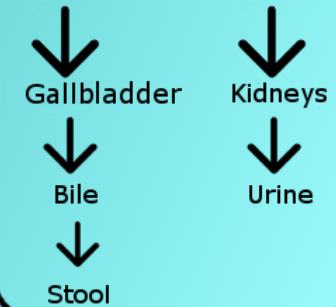
**Highly
Reactive**

Phase II
Required Nutrients

-Glutathione
-Amino Acids:
-Cysteine
-Glycine
-Glutamine
-Taurine
-Sulfur rich phytochemicals
-[eg. Onions, garlic & cruciferous vegetables]

Phase III

Eliminated via



Phase I Functions

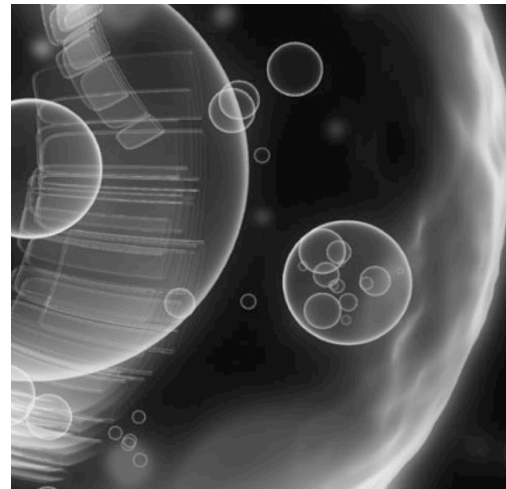
- Oxidation
- Hydrolysis
- Hydration
- Reduction
- Dehalogenation

Phase II Functions

- Acetylation
- Glucuronidation
- Amino Acid Conjugation
- Glutathione Conjugation
- Methylation
- Sulfation

Mitochondria Supplements

- A multi-step approach is needed to support mitochondrial health.
- An **Organic Acids Profile** helps to determine if there are any clinical foci in a patient's citric acid cycle that need to be resolved using the nutrients indicated by the testing.
- At the same time, employing certain mitochondria supplements can strengthen mitochondria that have been weakened by a poorly functioning citric acid cycle.





Specific Organic Acids

- If lactate is elevated on its own, without a coinciding pyruvate elevation, then CoQ10 deficiency should be strongly suspected.
- High citrate or isocitrate levels can indicate arginine insufficiency, which can indicate poor cardiovascular health and hypertension.
- High levels of succinate, fumarate, and malate are linked to low CoQ10 levels and fatigue, weakness, and neurological and myocardial degeneration.

www.functionalmedicine.net/pdf/Insider%27s%20Guide_37.pdf Accessed April 22, 2019

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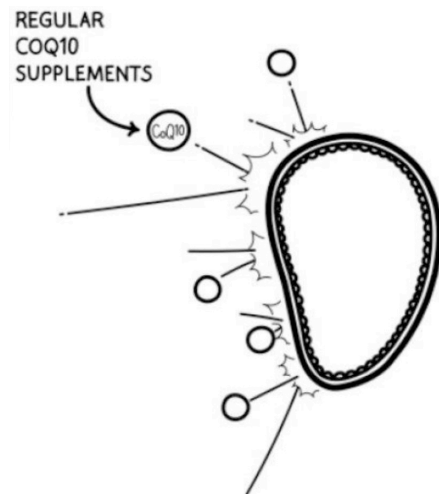
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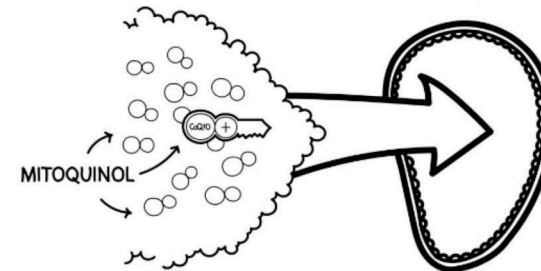
Foundational Mitochondrial Support

- There are many nutrients used to boost mitochondrial function.
- In my clinical practice, some of the ones I incorporate into my patients' regimens most often include NAD/NADH, MitoQ[®], CoQ10, and pyrroloquinoline quinone (PQQ).
- Coenzyme Q10 is integral to the functioning of the electron transport chain. It plays an important role in ATP production and is a ROS scavenger. **Because it can have low oral bioavailability, different forms were developed, MitoQ[®].**



CoQ10 vs MitoQ

What's the difference?



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MitoQ[®]

- MitoQ[®] is a shortened variation of the ubiquinol form of CoQ10 with the addition of an ion called **triphenylphosphonium, which gives the ubiquinol a positive charge.**
- This allows it to penetrate the mitochondrial membrane, creating enhanced absorption.
- Several studies have found MitoQ[®] improves endothelial function, reduces pulmonary hypertension, and has beneficial effects in fibromyalgia, as well as many other conditions.
- **MitoQ[®] penetrates and accumulates inside the mitochondria hundreds of times more effectively than all other forms of CoQ10 supplements.**

Acta Physiol (Oxf). 2018 Jan;222(1).

Eur Respir J. 2018 Feb 1. [Epub ahead of print.]

https://www.researchgate.net/publication/306032775_The_influence_of_Mitoq_on_symptoms_and_cognition_in_fibromyalgia_myalgic_encephalomyelitis_and_chronic_fatigue Accessed April 19, 2019



Nicotinamide Riboside Declines with Aging

- NADH supplements have a synergistic effect when combined with CoQ10 in reducing fatigue. **In a randomized, double-blind, placebo-controlled trial in 73 chronic fatigue syndrome patients, 200 mg/day of CoQ10 plus 20 mg/day of NADH resulted in a significant improvement of fatigue as well as markedly higher levels of NAD⁺/NADH, CoQ₁₀, ATP, and citrate synthase.**
- Converting food into energy
- Repairing damaged DNA
- Fortifying cells' defense systems
- Helps support internal circadian rhythm

Cell Metab. 2015;22(1):31–53.

F1000Res. 2018 Feb 1;7:132.

Antioxid Redox Signal. 2015 Mar 10;22(8):679-85.

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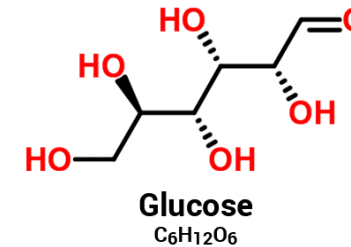
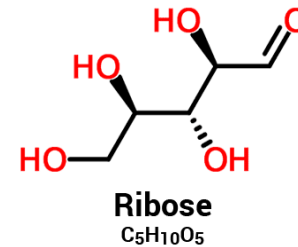
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D-Ribose and Mitochondrial Function

Supportive Roles:

- Increases ATP levels in heart cells and improves heart function
- Help with Fatigue and Fibromyalgia
- Muscular Strength
- Restless Leg Syndrome
- Neuroprotective



J Altern Complement Med. 2008 Nov;14(9):1165-6.
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PQQ- Pyrroloquinoline quinone

- **PQQ is an antioxidant that protects the mitochondria.** It has been found to improve cognitive function in humans, increase cerebral blood flow in the prefrontal cortex, and support healthy cholesterol levels.
- **PQQ stimulates mitochondrial biogenesis *in vitro*** by activating peroxisome proliferator-activated receptor (PPAR)- γ coactivator (PGC)-1 α , an important regulator of metabolism and mitochondrial oxidative defense.

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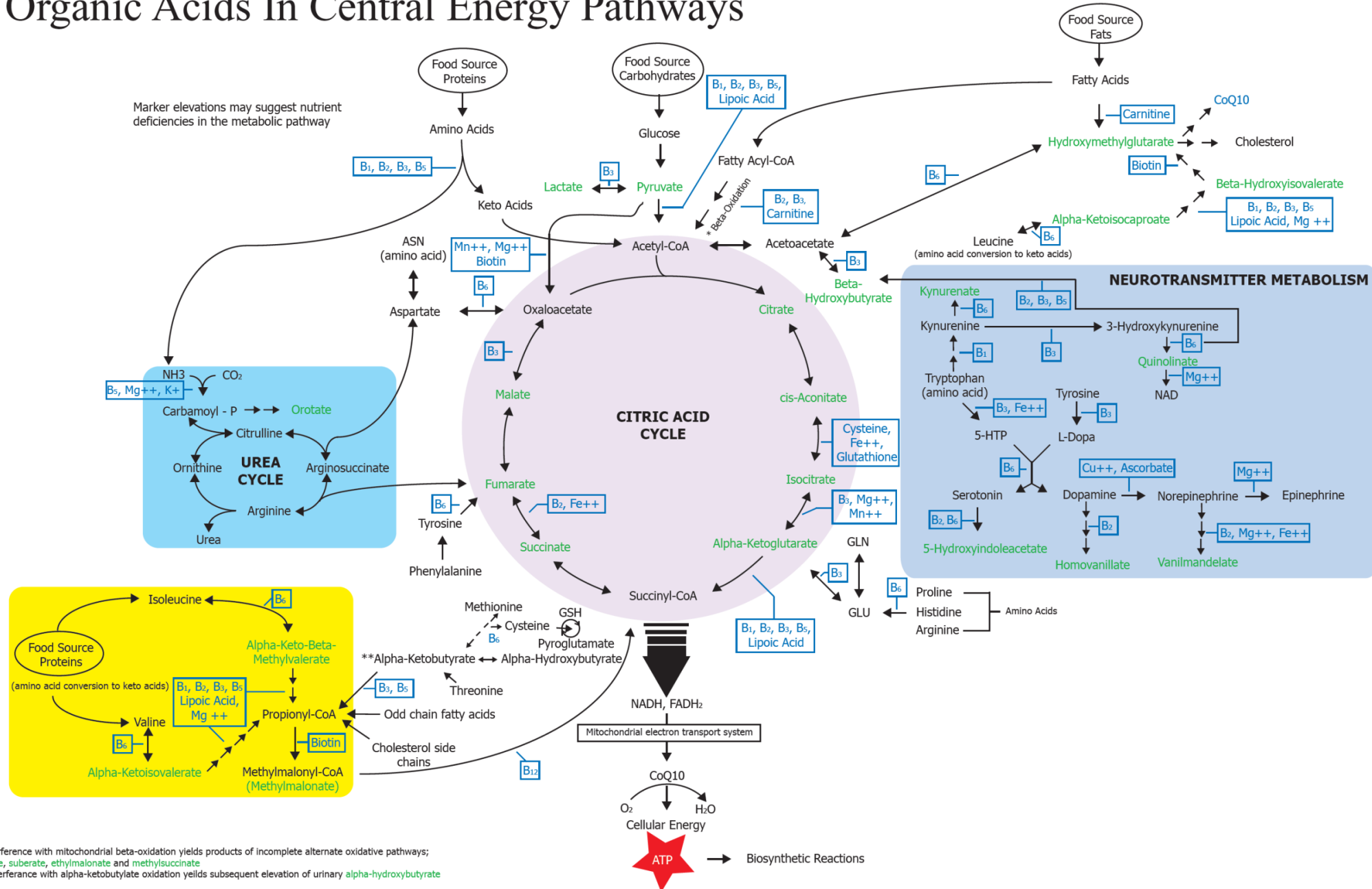
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Organic Acids In Central Energy Pathways



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* Interference with mitochondrial beta-oxidation yields products of incomplete alternate oxidative pathways; adipate, suberate, ethylmalonate and methylsuccinate
 ** Interference with alpha-ketobutyrate oxidation yields subsequent elevation of urinary alpha-hydroxybutyrate



Summary Message

A US BioTek Organic Acids Profile can reveal impairments in a patient's citric acid cycle and delineate which nutrients are needed to fuel this critical pathway properly.

Mitochondrial nutrients such as:

- Carnitine (various forms)
- MitoQ[®]
- NAD+
- PQQ
- Ribose
- Magnesium

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How “Charged Up” are your Patient’s Cells?



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Quantifying Patient Energy Pathways and Beyond

Organic Acids		
	Analytes Tested	Specimen
Organic Acids Profile (formerly known as UMP)	36	Urine
Environmental Toxins		
	Analytes Tested	Specimen
Environmental Pollutants Profile (EPP)	14	Urine
Organic Acids and EPP Combined Test	50	Urine

SINGLE URINE COLLECTION

A first morning mid-stream urine catch is easy for you to collect at home

NO REFRIGERATION OF SPECIMEN REQUIRED

Dried specimen is stable at room temperature for 55 days.

NO OVERNIGHT SHIPPING REQUIRED

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Q&A



Environmental Pollutant Profile - £130 RR

Organic Acids & Environmental Pollutants - £235 RRP

Organic Acids Profile - £196 RRP

Also available:

Sample reports / Quick guide / Nutrient source guide /
Metabolite guide / Organic acid flow chart



Thank you!

