# Cellular Cycle of the Energy Production and the Role of Mitochondrion.

# ETI Formulas to Support Body's Energy Field Structure and Functions.

It is an experimental fact of life that no living organism can survive without the energy that drives a cell's functions. Vertebrates lack the ability to obtain energy directly from the sun and must consume food to transform it into energy—that is, converting sugars, fats and proteins into adenosine triphosphate (ATP), which is utilized by cells as an energy source (McArdle et al. 2006).

## 1. Food Molecules Are Broken Down in Three Stages to Produce Adenosine Triphosphate (ATP)

The first step in the enzymatic breakdown of food molecules is digestion. Its final stage takes place either in our intestine's external cells or in the cell's lysosome, where the large polymeric molecules in food are broken down into their subunits—proteins into amino acids, polysaccharides into sugars, and fats into fatty acids and glycerol (Bender, 2007). After digestion, the small molecules derived from food enter the cytosol of the cell, where their oxidation initiates (Fig.1).

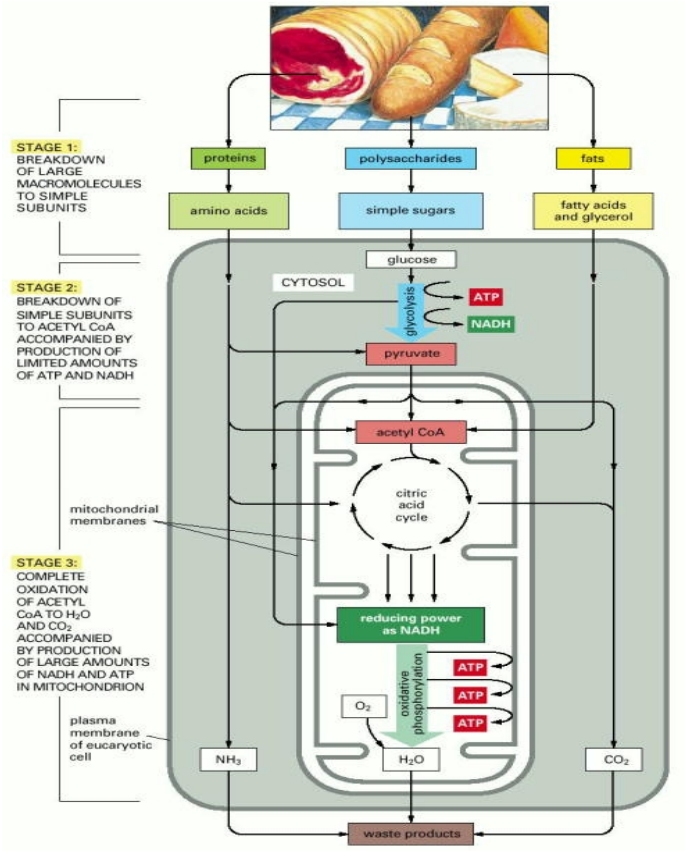



Fig 1.
From https://www.ncbi.nim.nih.gov/books/NBK2682

The second step of this process is a chain of reactions, called glycolysis, which converts each molecule of glucose into two smaller molecules of pyruvate. When oxygen is present, pyruvate is transported into the cell's power production center: mitochondria. There, each pyruvate molecule is converted into $CO_2$ plus a two-carbon acetyl group, which becomes attached to coenzyme A (CoA), forming acetyl-CoA, another activated carrier molecule. Large amounts of acetyl-CoA are also produced by the oxidation of fatty acids derived from fats, which are transported in the bloodstream, imported into cells, and then moved into mitochondria for acetyl-CoA production (Berg, Tymoczko, Stryer & Freeman, 2002).

The third step of the oxidative process takes place entirely in mitochondria. The acetyl group in acetyl-CoA is linked to coenzyme A through a high-energy linkage, and it is consequently easily transferable to other molecules. After its transfer to the four-carbon molecule oxaloacetate, the acetyl group enters a series of reactions called the *citric acid cycle* or Krebs cycle. It is precisely in these final steps that most of the energy released by oxidation is interconnected to produce the majority of the cell's ATP. (For more details, see Appendix 1. *Cellular Respiration of Glu*cose.)

The processes in the mitochondrion during steps 2 and 3 are too complex to be presented in the body of this text, but Appendix 2. *Electron Transport and Oxidative Phosphorylation* will

provide a description of the electron transport chain in the mitochondria and how this drives adenosine triphosphate (ATP) synthesis.

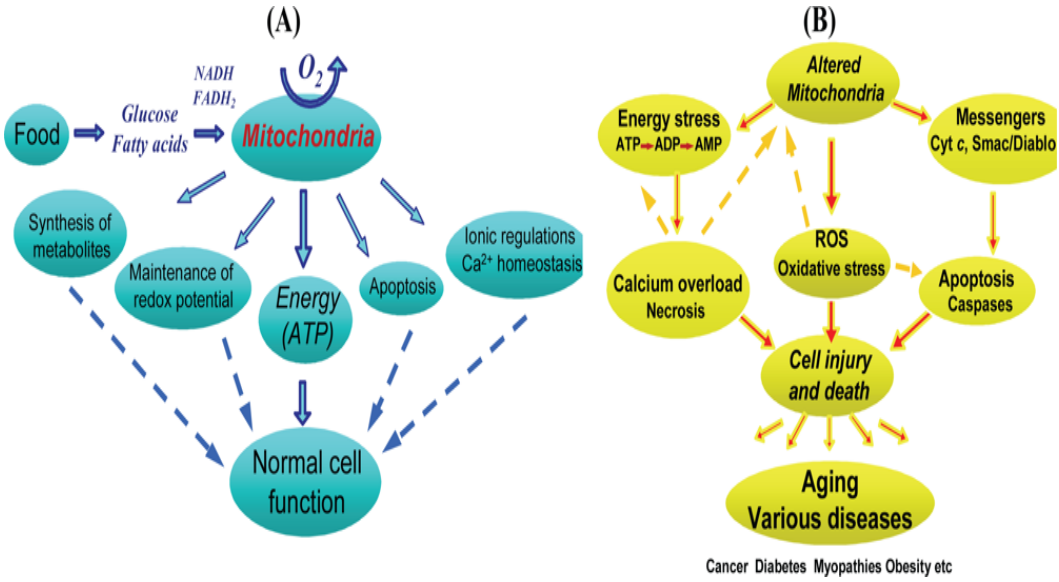
There is more to understand, however, about the breakdown of proteins used for energy production. Proteins are not a principal energy source, as the cell typically needs amino acids to provide the raw materials necessary to construct new proteins (Thompson & Manore, 2005). Only those amino acids that are not utilized in biosynthesis can be oxidized to generate metabolic energy. Most of their carbon and hydrogen atoms eventually form $CO_2$ or $H_2O$, whereas their nitrogen atoms are transported through various forms and eventually appear as urea, which is excreted (Campbell, Neil & Reece, 2008).

## 2. Mitochondrion Highlights

As described above, cells are able to perform tasks that consume energy by using chemical energy delivered in the form of a chemical compound called adenosine triphosphate (ATP), which is synthesized from the components adenosine diphosphate (ADP) and inorganic phosphate in a subcellular body called the mitochondrion (Scheffler, 2008).

Most animal cells contain between a few hundred and a few thousand mitochondria (Nisoli & Carruba, 2006). Mitochondria are found in the greatest numbers in the most metabolically active cells: neuron, heart and muscle cells (Manhanas, MacPherson & Tokatlidis, 2017), where mitochondria make up about 40% of cell volume (Nisoli & Carruba, 2006). Mitochondria are the only cellular organelles with their own DNA, and mitochondrial DNA (mtDNA) is derived almost entirely from the mother (Schon, DiMauro & Hirano, 2012). Current findings have uncovered that, in addition to being maternally inherited, mitochondrion can traverse cell boundaries and thus be horizontally transferred between cells (Torralba, Baixauli & Sanchez-Madrid, 2016).

The primary function of mitochondria is to produce ATP. (For more details, see Appendix 2). Recently, it has been acknowledged that mitochondria play a central role in the regulation of cells' apoptosis (Shoshan-Barmatz, De & Meir, 2017).

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Scientists also have shown that during aging, non-functional mitochondria defective in ATP production tend to accumulate, especially in the nervous and cardiac systems and skeletal muscles (Wilkins, et al., 2017; Lesnefsky, Chen & Hoppel, 2016; Seo, Lee, et al., 2016).

The data collected from brain analyses of patients with Alzheimer's disease have demonstrated a decrease in the activity of the mitochondrial electron transport chain, as well as a significant amount of oxidative damage. A depletion of the antioxidant systems, high markers of oxidative damage, is also present in those with Parkinson's disease (Mounton-Liger, et al., 2017; Wilkins, et al., 2017; Dai, et al., 2016).

The defective mitochondria have been shown to stay in the aged human heart, leading to oxidative injury and the activation of oxidants signaling cell death (Lesnefsky, Chen & Hoppel, 2016).

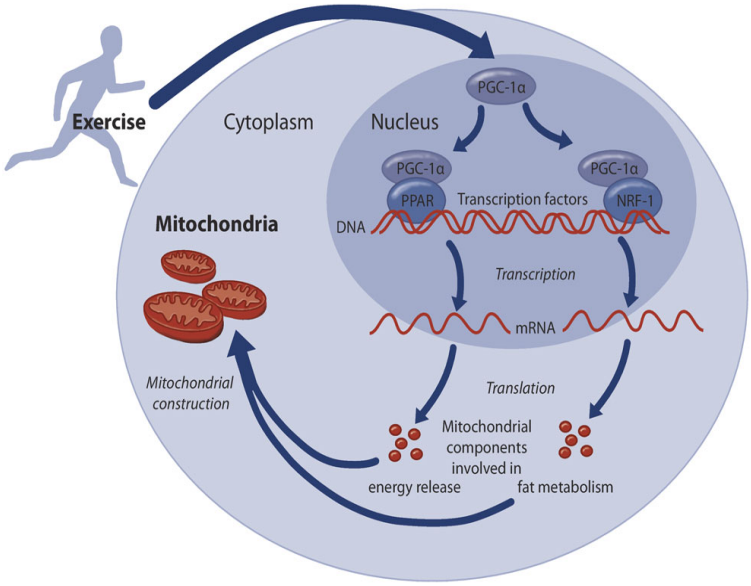
Current data also show that in prediabetic conditions, as well as in the predisposition to obesity, insufficient mitochondrial capability produces the accumulation of lipids inside the cells. In addition, it increases fat stored in muscle and liver cells, leading to the creation of abnormal patterns of taking glucose into the cells and the releasing of glucose by the liver (Montgomery & Turner, 2015).

## 3. Lifestyle Intervention to Support Energy Production

While the process of new mitochondria synthesis is complex (Alberts, et al., 2007), there are a few key activities responsible for the regulation of mitochondrial biogenesis.

**Exercise and Mitochondrial Biogenesis**

A significant amount of scientific data has confirmed increases in mitochondrial biogenesis in proportion to the amount of a person's physical activity (Carter, Chen & Hood, 2015; Reznik & Schulman, 2006; Coffey & Hawley, 2007; Baar, et al., 2002). Let's look more closely at the current evidence.



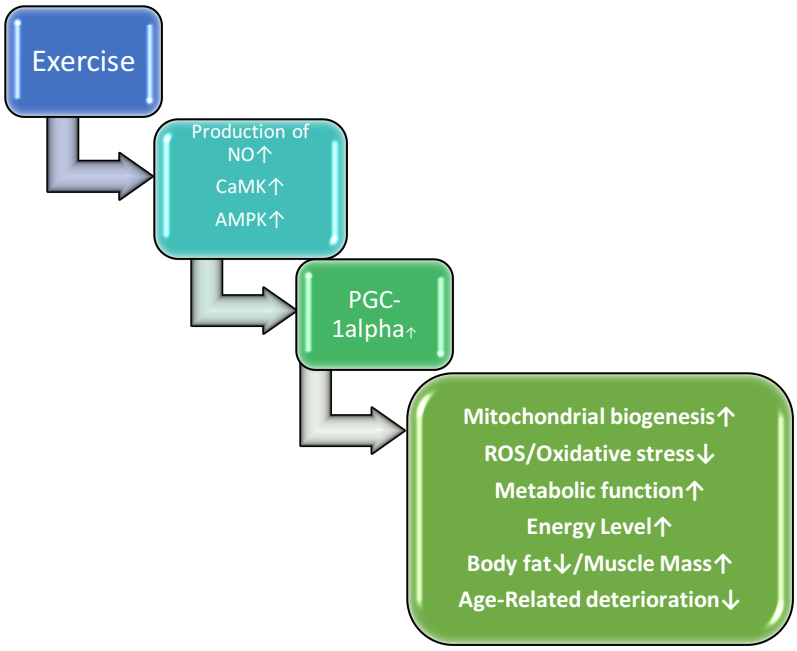

From http://www.scienceschool.org/2012/issue23/exerciseFrom

Mitochondrial biogenesis begins when exercise-related signals (some of them as calcium-calmodulin-dependent protein kinase (CaMK), 5' adenosine monophosphate-activated protein kinase (AMPK) and nitric oxide (NO)) activate the most important regulator of the mitochondrial production, PGC-1alpha (peroxisome proliferator-activated receptor-gamma activator – 1alpha) (Fernandez-Marcos & Auwerx, 2011; Ventura-Clapier, Garnier & Veksier, 2008).

Calcium plays a significant role in stimulating a direct metabolic response and begins the process of mitochondrial biogenesis. Research has demonstrated one of the calcium-activated enzymes, CaMK, increased during exercise, stimulates the uptake of glucose into the cells (Merry & McConell, 2009; Rose & Richter, 2005) and increases the production of PGG-1alpha, leading to mitochondrial biogenesis (Kusuhara, et al., 2007).

AMPK is an enzyme having an influence on the cellular adaptive reprogramming of metabolism, due to its ability to quickly activate or turn off metabolic pathways by being sensitive to dropping ATP levels (Canto & Auwerx, 2009). AMPK activation also has been shown to increase PGC-1alpha production with a following increase in mitochondrial biogenesis (Mihaylova & Shaw, 2011).

Many studies have demonstrated nitric oxide (NO) is involved in the mitochondrial biogenesis pathway, including in the control of mitochondrial respiration, apoptosis, free radical generation and, more recently, mitochondrial biogenesis, having PGC-1alpha as the main signaling molecule (Lira et al., 2010; Ghafourifar & Cadenas, 2005; Nisoli et al., 2003; Boveris et al., 2000).



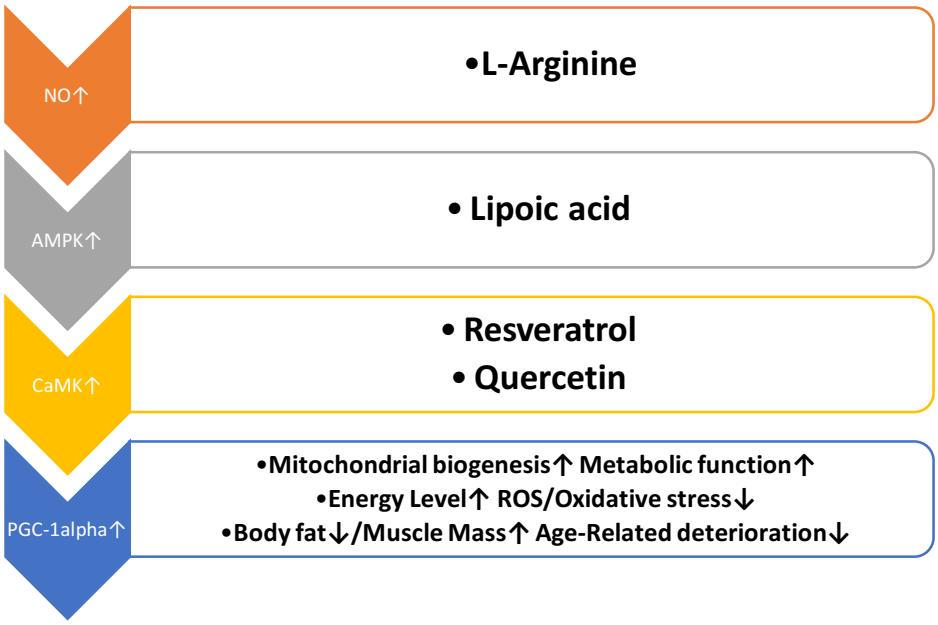

**Caloric Restriction**

The most widely accepted theory confirmed by experimental data is that a caloric restriction promotes healthy longevity by reducing damage to mitochondria from free radicals and other reactive oxygen species (ROS) (Indo, Davidson, Yen & et al, 2007; Ungvari, Paraddo-Fernandez & Csiszar, 2008; Lopez-Lluch et al., 2006). Recent data indicate the gene named *SIRT1* is increased with caloric restriction (Canto & Auwerx, 2009), as well as during exercise (Huang et al., 2016) and, further, *SIRT1* activates PGC – 1alpha (Canto & Auwerx, 2009).

## 4. Nutritional Intervention to Support Energy Production

The following material briefly describes nutritional interventions that stimulate pathways leading to mitochondrial biogenesis. Several experiments have shown the natural phenol and phytoalexin, resveratrol, activates *SIRT1*, AMPK and NO (Madrigal-Perez & Ramos-Gomez, 2016; Graback, Gawin & Pierzchalska, 2014). Quercetin, a plant polyphenol from the flavonoid group, is also able to activate *SIRT1* (Boost, Haenen & Bast, 2008). Based on recent experimental results, alpha-lipoic acid has been shown to increase AMPK in the periphery and decrease AMPK in the hypothalamus, leading to the recovery of a mechanism of weight control (Chen, Kang, Wang & Lee, 2012). All studies on animals show acute and chronic administration of L-arginine results in increased NO production, which leads to the improved blood flow and

vascular health (Preli, Klein & Herrington, 2002). Resveratrol activates NO, SIRT1, AMPK, but has very poor oral bioavailability (Venzel & Somoza, 2005).




## 5. ETI Formulas to Support Energy Production (Experimental Data with Peak Performance and Cells Longevity)

In an in vitro experimental case study conducted at Riga Technical University in Latvia (Klimaviciusa & Jekabsons, 2014), the ETI energy patterns Peak Performance and Cells Longevity demonstrated the capacity to support high viability and proliferation of cells in food deprivation conditions, even when mitochondrial poison was added to the media where cells grew. (For more information, see Appendix 3. *Effect of specific energy patterns on the vital functions of cells.*)

### Peak Performance, Quantum Balance and Oxygen Formulas Testimonials

Dr. Yury Kronn (2014), founder of Vital Force Technology, has said, "Obviously, we will not have clinical research on subtle energy effects until the mainstream scientific community recognizes the necessity to do it. Creative practitioners of energy medicine … achieved remarkable results in using energy medicine tools separately and/or in combination with other healing modalities." (For testimonials regarding Peak Performance, Quantum Balance and Oxygen formulas, see Appendix 4.)

### ETI Formulation to Support Energy Production and Energy Field Stability

As was mentioned in the previous chapters of the ETI educational program, practitioners have an opportunity to create a personalized approach for a particular client's energy needs with the use

of single ETI formulas, along with specific combinations of these formulas, and/or fine-tuning dosages, protocol and proportions. As Dr. Steven Davis has said, "Adding Vital Force Technology formulas to the treatment protocols provides the energetic fuel that gets the body moving in the right direction."

### 1. Increase Your Endurance and Recovery Energy Level

**Description:**

**The new ETI Endurance Formula** is intended to enhance mechanisms providing neurophysiological and energetic resources to the brain and body. It helps to regulate any allostatic overload, using several chemical and energetic mechanisms of action related to the hypothalamic-pituitary-adrenal axis (via synergistic activation of Siberian ginseng compounds, Peak Performance, Clear Mind and several other energy patterns). As a result, we have more efficient regulation of the body's energy production and its adaptive response, both within the brain and throughout the body. This formula can be used as a restorative tonic in cases of mental fatigue, poor concentration, overall weakness and lack of vitality, as well as before and/or after sports activities.

**Dosage:**
Dilute 1 ml of Endurance in 2-4 oz. of water. Drink 1-2 times per day or when it is necessary. It is an active energy pattern; do not drink it later than 3-4 hours before bedtime.

**Side Effects:**
No side effects, if used with the recommended dosages.

**Precaution**:
This formula contains a small amount of an herbal extract. Always consult with your healthcare practitioners, if you take medications or plan to have surgery.

### 2. Support Body's Performance and Oxygen Level

**Description:**
This formulation helps your body adapt quickly to any kind of physical activities, as well as supports it during recovery time, via energetically enhancing the broad physiological patterns connected to the body's energy production pathways.

**Formulation and Dosage:**
Combine Peak Performance (5-10 drops) and Oxygen Plus (3-5 drops) in 2-4 oz. of water. Drink as needed.

**Precautions:**
It as an active energy pattern. Do not use it later than 2-3 hours before bedtime.

### 3. Effective Support After a Long Work Day

**Description:**
This formulation may be used to enhance one's ability to regulate, regenerate, adapt and increase vitality after prolonged mental and/or physical activities.

**Formulation and Dosage:**
Combine Peak Performance (5-10 drops) and Clear Mind (3-5 drops) in 2-4 oz. of water. Drink as needed.

**Precautions:**
No side effects or precautions, if used within the recommended dosages.

## Future ETI Formulas to Stimulate Energy Production

ETI and VFT are constantly working in the direction of improving and/or bringing to the customers new formulas that show themselves to be effective in supporting the body's energy field and its anti-aging potential. The following formulas will be presented to ETI customers in 2018: Perfect Vitality, Mitochondria Support, Cells Longevity.

## Appendix 1. Cellular Respiration of Glucose

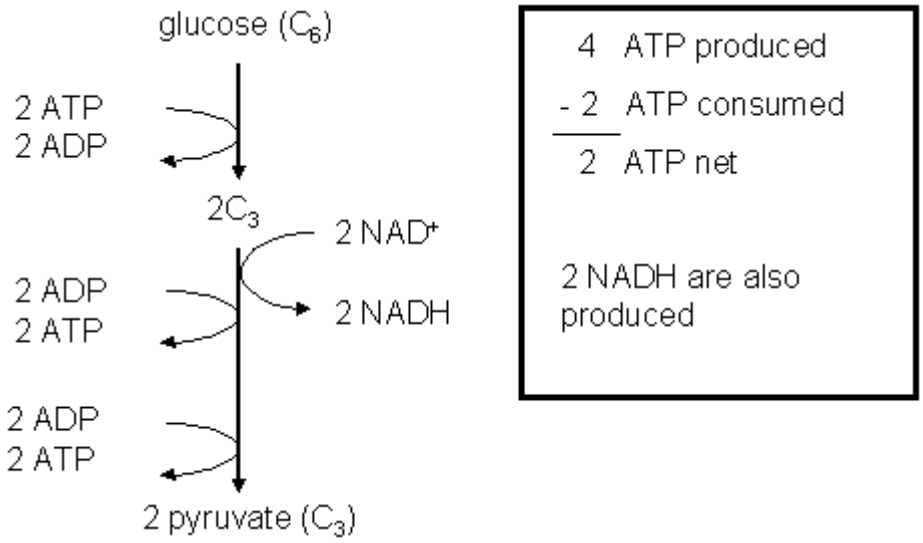
Cellular respiration allows organisms to use energy stored in the chemical bonds of glucose ($C_6H_{12}O_6$).

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{energy (36 ATP)}$$

The complete breakdown of glucose to carbon dioxide and water requires glycolysis and aerobic respiration. Glycolysis produces two ATP. Thirty-four more ATP are produced by the aerobic pathways if oxygen is present. In the absence of oxygen, fermentation reactions produce alcohol or lactic acid but no additional ATP.

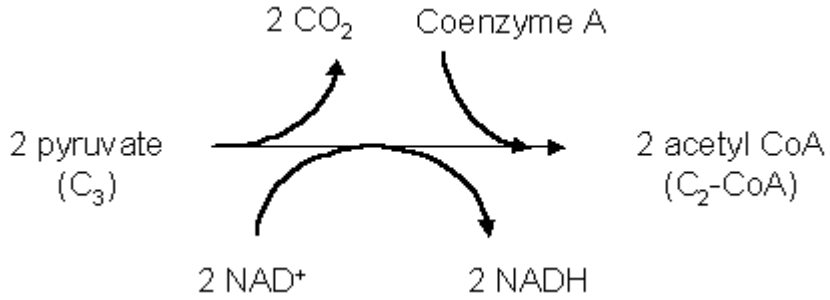
Glycolysis

Glycolysis occurs in the *cytoplasm* and does not require oxygen. There are ten steps in glycolysis and each one is catalyzed by a specific enzyme. A brief summary of these reactions is as follows: two ATP molecules are used to phosphorylate and activate compounds that will become converted to pyruvic acid; two hydrogen atoms are removed by NAD+ forming two NADH; additional phosphorylation results in intermediate 3-carbon molecules with two phosphate groups. The net yield of ATP in glycolysis is two for each glucose molecule (two are used, but four are produced).



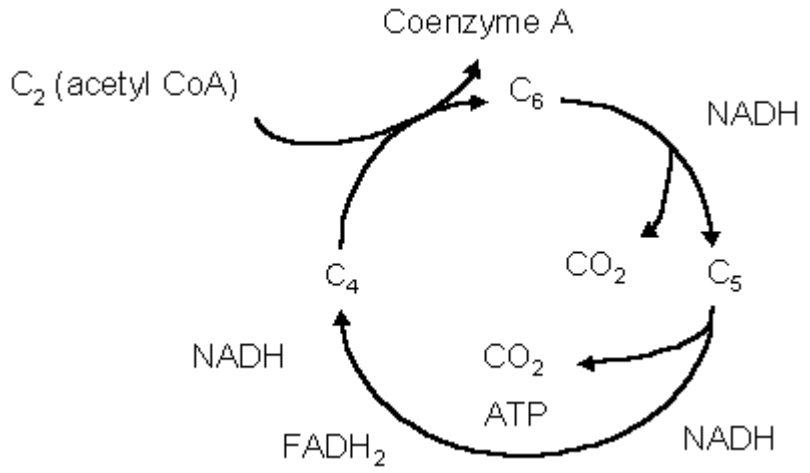

Formation of Acetyl CoA

Pyruvate produced by glycolysis enters the mitochondrion and is converted to ***acetyl CoA*** by the reaction shown below. The two-carbon compound produced is attached to Coenzyme A to produce acetyl CoA.




Krebs Cycle

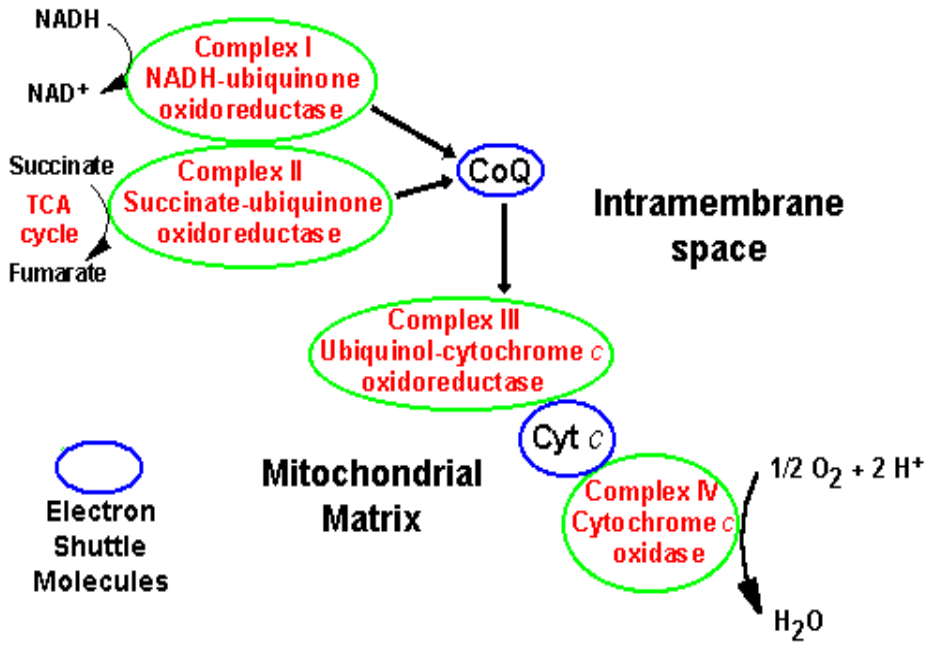
The Krebs cycle can be summarized by the diagrams below. The diagram occurs twice, once for each acetyl CoA.




When acetyl CoA attaches to a $C_4$ molecule in the Krebs cycle, the Coenzyme A is released. Two acetyl CoA molecules are consumed to produce 4 $CO_2$, 2 ATP, 6 NADH and 2 $FADH_2$. The ATP molecules are produced by substrate level phosphorylation.

## Appendix 2. Electron Transport and Oxidative Phosphorylation

The respiratory chain ("electron transport chain") attached to the inner wall of the inner membrane is composed of 4 protein complexes. These protein complexes are identified as Complex I, II, III and IV.



Complex I and Complex II independently supply electrons to Complex III, which supplies electrons to Complex IV. The soluble carrier transporting electrons from Complex I and II to Complex III is CoQ (CoQ10 in human). Thus, statins inhibit the synthesis of CoQ, and it is possible to say there are potential side effects of statins.

The soluble carrier that transports electrons from Complex III to Complex IV is cytochrome c. Complex IV combines its electrons (which are actually hydrogen atoms) with oxygen to form water. The energy released by the oxidations in the respiratory chain is used to pump protons outside the inner mitochondrial membrane.

If you block electron transport, you block the formation of the proton gradient and therefore block the supply to produce ATP (uncoupling agents). The first weight loss drug was the uncoupling agent, bringing several fatalities and cataracts. Several pesticides inhibit the transport of electrons to Complex I, as well as carbon monoxide. The antibiotic oligomycin inhibits ATP production by blocking the pore through which the protons pass.

Scientific data has shown the mtDNA genes are of value in providing a rapid local synthesis of proteins required for oxidative phosphorylation. Oxidative stress, due to insufficient oxidative phosphorylation capability, could signal mitochondrial transcription factors to induce production of mtDNA-coded proteins, which are then implanted into the inner membrane where they attract the nDNA-coded proteins required for complete assembly of the complexes.

Complex I, which has seven mtDNA-coded proteins, ages most rapidly. Substantial nigra neurons have increased susceptibility to Complex I defects, which may be responsible for Parkinson's disease. By contrast, Complex II (which has no mtDNA-coded proteins) and Complex III (which has only one) are relatively unaffected by aging. Cytochrome c oxidase (between Complex III and Complex IV) activity declines with age, resulting in increased production of superoxide and hydrogen peroxide.

An estimated 1–2% of oxygen used by mitochondria will normally "leak" from the respiratory chain to form superoxide. The pro-inflammatory cytokine Tumor Necrosis Factor–alpha (TNF–α, associated with the metabolic syndrome) induces increased free radical production from the respiratory chain. Free radicals can damage the mitochondrial inner membrane, creating a positive feedback loop for increased free radical creation. The most damaged mitochondria are consumed by lysosomes, whereas the more defective mitochondria (which produce less ATP, as well as less superoxide) remain to reproduce themselves. The efficiency of lysosomes to consume malfunctioning mitochondria declines with age, resulting in more mitochondria producing higher levels of superoxide. Mitochondria of older organisms are fewer in number and larger in size.

The greatest damage occurs in the mitochondria themselves, including damage to the respiratory chain protein complexes (leading to higher levels of superoxide production), damage to the mitochondrial membrane (leading to membrane leakage of calcium ions and other substances) and damage to mitochondrial DNA (leading to further damage to mitochondrial protein complexes). Mutations in mtDNA occur at 10-20 times the rate seen in nuclear DNA. Unlike

nuclear DNA, mtDNA has no protective histone proteins. And DNA repair is less efficient in mitochondria than in the nucleus.

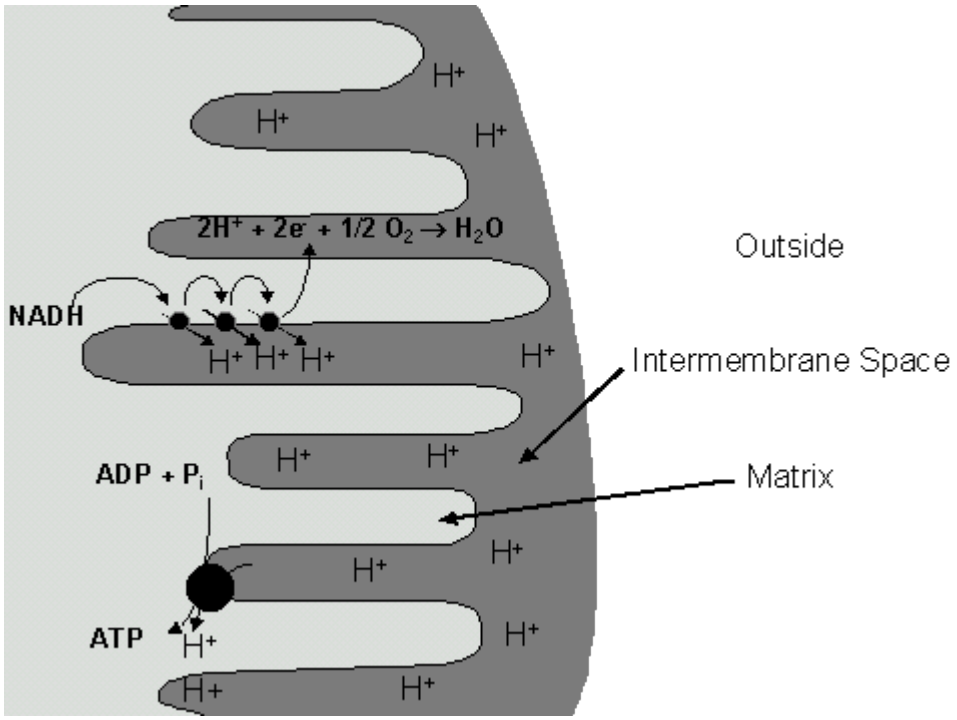
Acetyl CoA formation and the Krebs cycle occur in the inner space of mitochondria, called the matrix. The space outside the inner membrane is the intermembrane space. The electron transport system pumps hydrogen ions ($H^+$) into this space for oxidative phosphorylation.

Oxidative Phosphorylation

NADH or FADH2 bring electrons to the electron transport system of the mitochondrion. This system contains membrane-bound electron carriers that pass electrons from one to another. When a carrier reduces another, some of the energy that is released as a result of that reduction is used to pump hydrogen ions across the membrane into the intermembrane space. The remaining energy is used to reduce the next carrier.

Because of this electron transport system's function, hydrogen ions become concentrated in the intermembrane space. These concentrated ions contain energy, creating a kind of barrier. The enzyme ATP synthase is able to use the energy of this osmotic gradient to produce ATP, as the hydrogen ions move under osmotic pressure through the enzyme back into the matrix of the mitochondrion.

As was observed earlier, oxygen is the final electron acceptor. The low-energy electrons that emerge from the electron transport system are taken up by O2. The negatively charged oxygen molecules take up protons from the medium and form water ($2H^+ + 2e^- + 1/2\ O_2$ -> H2O).



## Appendix 3. Effect of Specific Energy Patterns on the Vital Functions of Cells

An experiment on the cell viability and mitochondrial membrane potential under a "food deprivation" condition, including the presence of strong mitochondrial toxins, was conducted at Riga Technical University in Latvia in 2013.

The human embryonic kidney cell line (HEK-293) was used in the research. On the first day, cells were grown in 96-well plates (100 mcl/well) using a medium (DMEM/GlutaMAX-1) containing 10% fetal bovine serum (FBS). On the second day, the medium and serum in the plates were changed: the experimental plates with medium and serum infused with "Cell Longevity" or "Peak Performance." The control used the regular medium and serum. On the third day, the media were changed again to the same media without PBS, in order to create serum deprivation conditions that lasted for the next three days before testing. Then, cell viability was tested by the MTT colorimetric assay, using the Tecan spectrometer. The cell viability of the control cultures was taken as 100%.

Results of a comparison of the cells grown in energy-infused media and the control are presented in Fig. 1. The "Cell Longevity" energy pattern, like in the previous experiment, produced the best effect on cell viability – 46% higher than in the control; and "Peak Performance" showed a 21% increase in comparison with the control.

The next experiment was done with the addition of mitochondrial toxins (on top of serum deprivation). Two well-known types of toxins were used: $MMP^+$ (1-methyl-phenylpyridine) and Rotenone (Fig. 2 and 3).

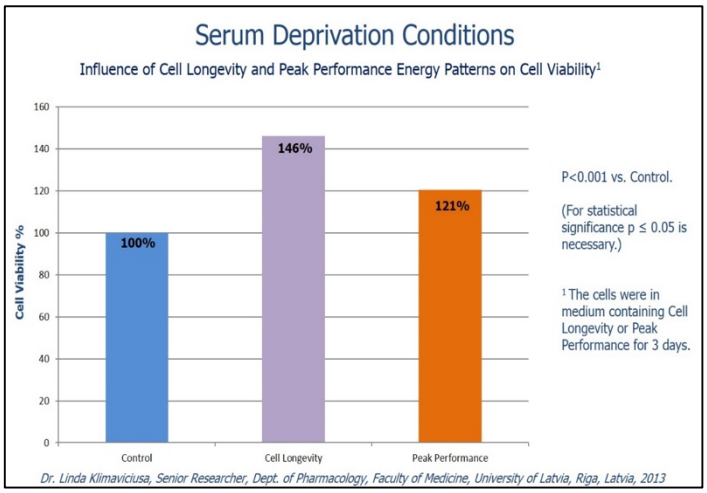



Fig. 1

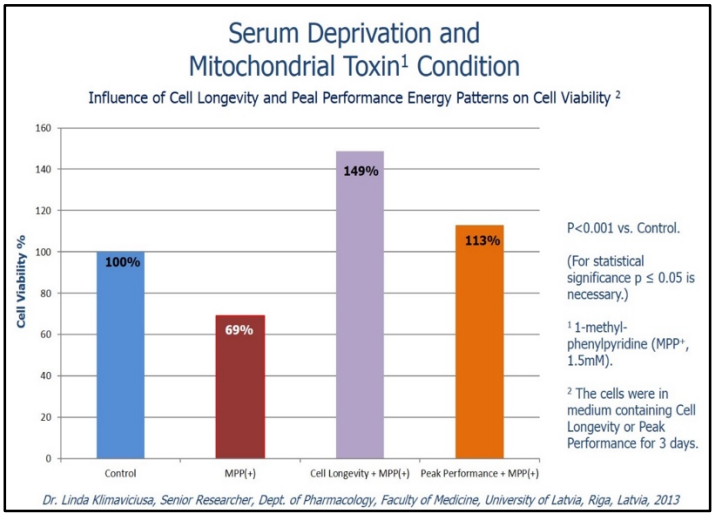



Fig.2

One can see in Fig. 2 that, in the infused media the viability of cells was better, not only in comparison with the control containing mitochondrial poison, but even in comparison with the non-poisoned control, for both energy patterns.

In the case of the presence of Rotenon toxin (Fig. 3), "Cell Longevity" provided cellular viability better than in the non-poisoned control, while the "Peak Performance" energy pattern provided cellular viability equal to that of the control cells.

Fig. 4 demonstrates the result of measuring mitochondrial membrane potential in media containing $MMP^+$ poison and infused with "Cell Longevity" or "Peak Performance," in comparison with non-infused controls. Measurements show cells in energy-infused media had higher membrane potential than even the non-poisoned control with regular growth media.

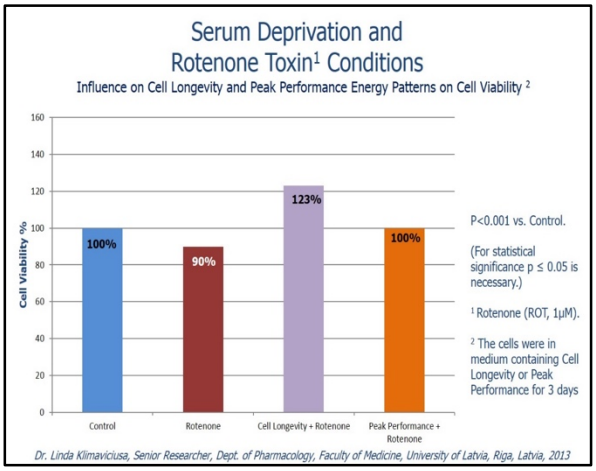



Fig. 3

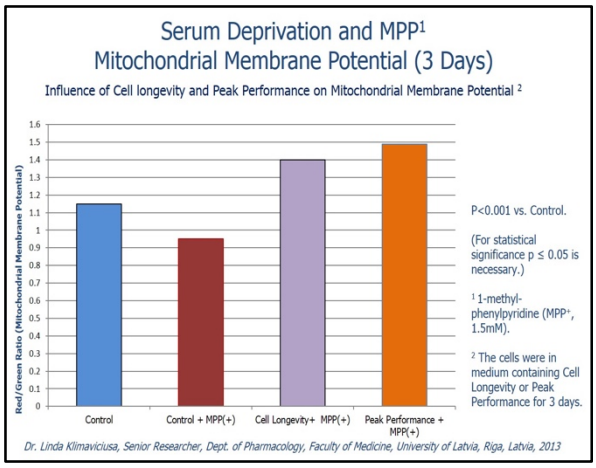



Fig. 4

This research clearly demonstrated subtle energy patterns targeted for the support of cellular health reveal an extraordinary ability to provide high viability and proliferation of cells in food deprivation conditions, even when mitochondrial poison was added to the media where cells grew.

## Appendix 4. Testimonials Concerning Energy Formulas Peak Performance, Oxygen, Oxygen Plus and Quantum Balance

"I have used Energy Tools' *Oxygen Plus* and *Peak Performance* to enhance my running. I could barely run a mile and now I'm running 3.5 miles daily, and getting faster! I use these products with clients who love the results even when they don't understand how it works." – Dr. Robert P.

"What I've also noticed from the *Peak Performance* is that it improves an athlete in three main ways: 1) overall endurance and aerobics; 2) greater power/immediate strength gains, and: 3) importantly, a more determined focus and a mental alert …" – Tim T.

"I used these products during and at the end of the season mountain bike series. I went from being just able to finish to win the last race of the year. I felt as though I could go harder than ever before. I ended the season 6th overall." – Glenn W.

"So far, all the testing I've done with athletes with the *Quantum Balance* has been unbelievably positive. We are finding ourselves able to climb harder for longer without as much fatigue. I've also been noticing the recovery time is improving!" – Tim T.

"I like the *Oxygen* and the *Peak Performance*. I feel like something is happening but I don't know what. I have been climbing strong though every day I use them. I put 10 drops of each in my water bottle." – Ted R.

"My performance on the indoor climbing training wall has improved greatly using those drops *Peak Performance* and *Oxygen Plus.*" – Matt W.

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