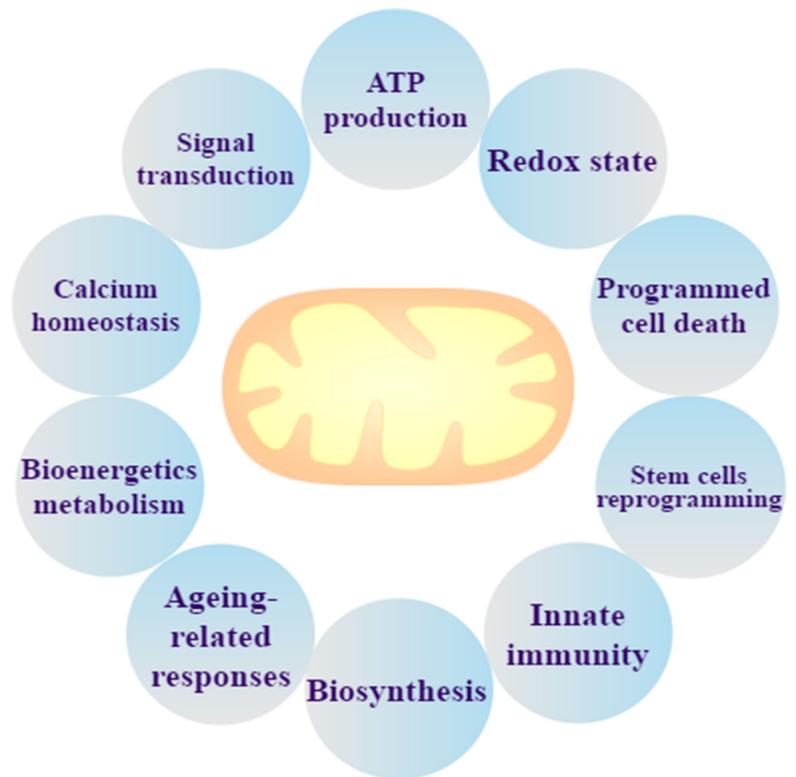


# What's Up Doc?

## The relationship between AMPK, ATP, Mitochondria and cellular survival

Recent research is demonstrating the importance of mitochondria and how mitochondrial dysfunction is the cause of many age-related challenges, including energy levels, immune dysregulation, and cognitive decline. Every one of the trillion plus cells in your body contains 2,000 to 2,500 mitochondria per cell! Our mitochondria are responsible for converting the nutrients we eat into energy which in turn powers our cells so we can perform at our peak function. Compared to a whole cell, the tiny mitochondria that lives within the larger cell, is highly susceptible to free radical damage from stress, dietary elements and more. As we age mitochondrial stress results in the decline of mitochondrial energy and function. This month we have a look at mitochondria.



The relationship between Adenosine

Triphosphate (ATP), AMP-activated protein kinase (AMPK), and mitochondria is central to cellular energy management and overall health. Mitochondria are the primary sites for ATP generation via oxidative phosphorylation, effectively acting as the cell's energy producers. ATP is the immediate energy currency; when it is consumed, it is converted to ADP and subsequently to AMP, signaling an energy deficit. This rise in the AMP/ATP ratio directly activates AMPK, which functions as the master energy sensor of the cell. Once activated, AMPK orchestrates a metabolic shift: it switches off ATP-consuming anabolic pathways (like lipid synthesis) and switches on ATP-generating catabolic pathways (like fatty acid oxidation) to restore energy balance. Most importantly, AMPK promotes mitochondrial biogenesis—the creation of new mitochondria, by activating the transcriptional coactivator PGC-1. This process increases the cell's capacity for ATP production. AMPK regulates mitochondrial quality control by promoting mitophagy (the selective degradation of damaged mitochondria). The importance of this triad lies in its role as a feedback loop: low ATP activates AMPK, which then signals the mitochondria to either produce more energy or clear out dysfunctional components, ensuring sustained cellular viability, metabolic flexibility, and protection against conditions linked to energy imbalance, such as metabolic syndrome and aging.

### Adenosine triphosphate (ATP)

Adenosine triphosphate (ATP) is the primary energy currency of the cell, essential for various biological processes. Composed of adenosine and three phosphate groups, ATP stores energy in the high-energy bonds between its phosphate groups. When energy is needed, ATP can be hydrolyzed to adenosine diphosphate (ADP) and inorganic phosphate, releasing energy that powers cellular functions such as muscle contraction, protein synthesis, and active transport

across cell membranes. ATP is continuously regenerated through cellular respiration in mitochondria, making it vital for maintaining cellular health, metabolism, and overall physiological function.

### **AMPK (AMP-Activated Protein Kinase)**

AMPK (AMP-activated protein kinase) is an essential energy-sensing enzyme that regulates cellular energy homeostasis. Found in various tissues, including the liver, skeletal muscle, and adipose tissue, AMPK is activated when energy levels are low, specifically when the AMP/ATP ratio increases. Upon activation, AMPK promotes catabolic pathways that generate ATP, such as glucose uptake and fatty acid oxidation, while suppressing anabolic pathways that require energy, such as lipid and protein synthesis. This regulatory role makes AMPK a critical player in metabolic health and a potential target for interventions in conditions like obesity and type 2 diabetes.

### **Mitochondria**

Mitochondria are double-membrane-bound organelles known as the powerhouses of the cell. Mitochondria are essentially the "biological intersection" where environment meets epigenetics. Beyond their textbook definition as "powerhouses," mitochondria function as the primary metabolic sensors of the cell, integrating signals from nutrition, light, stress, and toxins to dictate cellular fate.

### **Energetic Currency and The Krebs Cycle (TCA)**

At the core of mitochondrial function is the production of adenosine triphosphate (ATP) via the Electron Transport Chain (ETC). This is the foundation of our vitality.

**Substrate Flexibility:** Mitochondria determine how efficiently a patient switches between glucose and fatty acids (metabolic flexibility).

**The Krebs Cycle (TCA):** This cycle provides the precursors for heme synthesis and amino acid metabolism, making mitochondrial health central to addressing anemia and neurotransmitter imbalances.

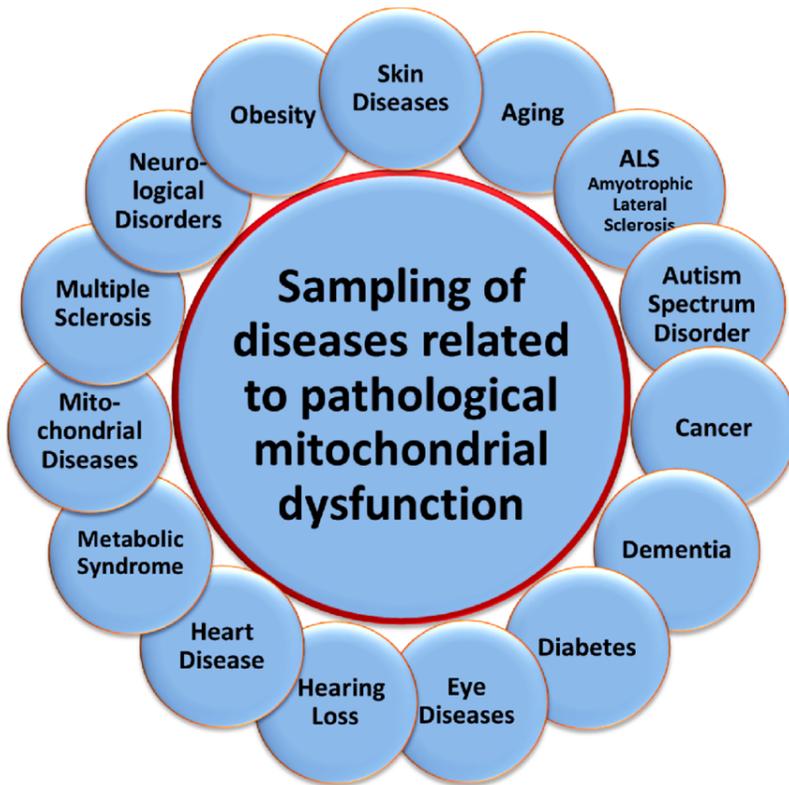
### **The Cell Danger Response (CDR)**

Modern naturopathic research, spearheaded by Dr. Robert Naviaux, suggests that mitochondria have a secondary, perhaps more critical role: **Defense**.

When mitochondria sense a threat (viral, chemical, or emotional stress), they shift from energy production to **cellular defense**. This "Cell Danger Response" stiffens the cellular membrane and halts oxidative phosphorylation. If the "threat" becomes chronic, the patient experiences **Chronic Fatigue Syndrome** or systemic inflammation because the mitochondria refuse to "turn the lights back on" until safety is perceived.

### **Redox Balance and Signaling**

Mitochondria are the primary source of Reactive Oxygen Species (ROS). While often viewed negatively, these free radicals serve as vital **signaling molecules**:



**Mito hormesis:** Small amounts of oxidative stress (from exercise, fasting, or phytonutrients like sulforaphane) trigger the Nrf2 pathway, upregulating endogenous antioxidants like glutathione.

**Apoptosis:** Mitochondria act as the "judge and executioner" for the cell. By releasing Cytochrome C, they initiate programmed cell death, a process crucial for preventing oncogenesis and clearing senescent cells.

**Steroidogenesis and HPA-Axis Integration**  
A point often overlooked in conventional medicine but vital for hormone balancing: **the first step of steroidogenesis happens inside the mitochondria.** The conversion of cholesterol to pregnenolone by the enzyme

occurs on the inner mitochondrial membrane. If a patient has mitochondrial dysfunction (due to nutrient deficiencies like CoQ10, Magnesium, or B-vitamins), no amount of adrenal support will fully resolve their "hormonal fatigue" because the raw materials aren't being processed at the source.

### The Calcium Buffer

Mitochondria work in tandem with the Endoplasmic Reticulum (ER) to sequester and release calcium ions. The role of mitochondria and the ER is key in managing calcium ion dynamics, which are crucial for several physiological processes, including muscle movement, neuronal communication, and maintaining heart rhythm. This interplay is essential for effective cellular function and overall health.

### References

- [Keeping the home fires burning: AMP-activated protein kinase - PMC](#)
- [AMPK, Mitochondrial Function, and Cardiovascular Disease - MDPI](#)
- [AMPK, Mitochondrial Function, and Cardiovascular Disease - PubMed](#)
- [AMPK: guardian of metabolism and mitochondrial homeostasis - PMC](#)
- [AMPK and Mitochondria: Key Regulators of Energy Balance - Amerigo Scientific](#)
- [AMP-activated protein kinase: function and dysfunction in health and disease - PMC](#)

## SUPPORT.

### B STRESS COMPLEX: Dose 1 -3 Per Day

A 100% vegetarian whole food B vitamin complex. Devoid of any synthetic or isolated ingredients. The B vitamins are key for mitochondria function, ATP, and AMPK.

**B1 (Thiamine):** Essential for carbohydrate metabolism and the synthesis of ATP, a key energy source for mitochondria. Indirectly influences AMPK activation through improved glucose uptake.

**B2 (Riboflavin):** Plays a crucial role in the electron transport chain, allowing efficient ATP production. Facilitates the conversion of nutrients which contributes to ATP synthesis and stimulates AMPK.

**B3 (Niacin):** Key component of NAD and NADH, which are critical cofactors in mitochondrial energy production. The increase in NAD<sup>+</sup> activates AMPK through energy sensing mechanisms. B3 critical for ATP production in cellular respiration.

**B4 (Adenine):** Adenine, often referred to as vitamin B4, is a purine nucleobase that plays a vital role in various biological processes. Although not classified as an essential vitamin, adenine is crucial for cellular functions, including the synthesis of nucleotides, which are the building blocks of DNA and RNA. This makes adenine essential for cell growth, reproduction, and overall energy metabolism, as it is involved in the formation of adenosine triphosphate (ATP), the primary energy carrier in cells.

**B5 (Pantothenic Acid):** Important for synthesizing coenzyme A, which is involved in fatty acid metabolism, AMPK activation, and ATP generation.

**B6 (Pyridoxine):** Supports amino acid metabolism and neurotransmitter synthesis, indirectly affecting energy metabolism and ATP synthesis.

**B7 (Biotin):** Involved in various metabolic processes, including fatty acid synthesis and energy production, which aids mitochondria function and ATP production.

**B12 (Cobalamin):** Essential for fatty acid metabolism and DNA synthesis; the metabolic pathways that convert fatty acids and amino acids into energy support ATP production. B12 deficiencies can lead to mitochondrial dysfunction.

### **CoQ10-Cardio: Dose 2 - 6 per day.**

CoQ10-Cardio is a combination of vitamin C, herbs, and plant sourced ubiquinone CoQ10 of which each capsule contains 50mg. CoQ10 is an essential cofactor in the electron transport chain (ETC). It facilitates the transfer of electrons, which is crucial for ATP synthesis. CoQ10 enhances ATP production. CoQ10 acts as a potent antioxidant, protecting mitochondrial membranes from oxidative stress. CoQ10-cardio also includes 18mg of food vitamin C per capsule from acerola cherries another powerful antioxidant. Lastly, CoQ10 has been shown to stimulate mitochondrial biogenesis through the activation of nuclear transcription factors such as PGC-1 $\alpha$  (peroxisome proliferator-activated receptor gamma coactivator 1-alpha). Increased mitochondrial biogenesis enhances energy capacity and improves metabolic health, particularly in conditions like obesity, type 2 diabetes, and neurodegenerative diseases.

### **Dual Vitality: Dose 2 - 4 per Day**

The combined effects of Organic Cordyceps and American Ginseng contribute to improved mitochondrial function through enhanced ATP production, reduced oxidative stress, improved



energy metabolism, and overall cellular health. These benefits translate into better physical performance, increased energy levels, and greater resilience against age-related mitochondrial decline.

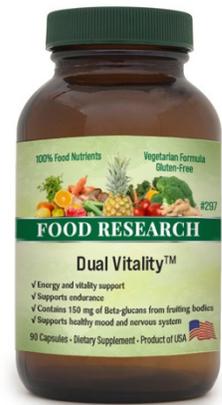
Cordyceps has been shown to increase the production of adenosine triphosphate (ATP), the primary energy currency in cells, which is crucial for optimal mitochondrial function. Enhanced ATP synthesis directly translates to better energy availability for cellular processes. Cordyceps activates AMP-activated protein kinase (AMPK), an important regulator of cellular energy homeostasis. AMPK activation encourages mitochondrial biogenesis (the production of new mitochondria) and improves overall metabolic health. Finally, Cordyceps enhances oxygen uptake during exercise improving aerobic capacity and energy metabolism leading to better mitochondrial function during physical activity.

American Ginseng is recognized for its adaptogenic properties. Its effects on mitochondrial function include

Supporting mitochondrial energy production. Increased energy can help maintain mitochondrial activity and efficiency.

The ginsenosides found in American Ginseng improve glucose metabolism, which leads to more efficient mitochondrial ATP production. Improved glucose utilization enhances energy supply for mitochondrial functions.

American Ginseng has anti-inflammatory and antioxidant properties both of which are essential to maintain the vitality and health of mitochondria.



## Premier Labs NADH Dose at 2 per day



NADH (nicotinamide, adenine, dinucleotide) is an essential coenzyme found in all living cells, playing a crucial role in energy metabolism. NADH is a reduced form of NAD<sup>+</sup>, a key player in redox reactions in the body. It acts as an electron carrier in the electron transport chain (ETC) within mitochondria, which is essential for ATP production. By facilitating the transfer of electrons derived from nutrients (carbohydrates, fats, and proteins) to the ETC, NADH supports aerobic respiration, leading to ATP synthesis. By providing additional NADH, the supplement can enhance mitochondrial function, improving the efficiency of the electron transport chain. This leads to increased ATP production as mitochondria convert nutrients into energy more effectively. With more NADH available, the Krebs cycle operates more efficiently, directly increasing the amount of ATP generated. Enhanced mitochondrial function due to increased NADH leads to better cellular energy

balance, which modulates AMPK activity, ultimately affecting metabolism and various physiological processes. Each capsule contains 10mg of NADH

## Premier Labs PQQ Complex Dose at 2 per Day

PQQ Complex with CoQ10 features PQQ (pyrroloquinoline quinone), a unique B vitamin-like nutrient. It offers nerve, cardiovascular and cognitive (learning and memory) support. This formula is coupled with natural source, fermented CoQ10 (trans isomer form) which promotes cellular energy and offers antioxidant support.

PQQ is an antioxidant with the ability to activate cell signaling pathways directly involved in promoting mitochondrial energy metabolism as well as reinforcing the mitochondria's limited

defenses and thus promote the health of mitochondrial DNA. In addition to PQQ the formula includes live-source, fermented CoQ10. This CoQ10 is produced through a natural fermentation process which yields 50 mg/capsule of the highly bioavailable, preferred trans isomeric form of CoQ10. The natural trans-isomer of CoQ10 is the most desirable because it is identical to the CoQ10 produced by all the cells in the body. The level of our cellular health is in direct proportion to the mitochondria's ability to neutralize two key interacting forces that it is regularly exposed to: free radical stress and excitotoxicity. Poor mitochondrial response can lead to devastating effects on the heart and brain and potentially, all the cells of the body. PRL's PQQ is a clean synthetic and excipient free way to achieve this.



## Key Interactions Between the Microbiome and Mitochondria

The relationship between the microbiome and mitochondria is a complex and significantly impacts our health and metabolism. Here's an insight overview of how these two systems interact:

### Metabolism and Energy Production

**SCFAs:** The gut microbiome ferments dietary fibers into short-chain fatty acids (like butyrate, propionate, and acetate), which provide energy to colon cells and can enter the bloodstream to enhance mitochondrial function in peripheral tissues.

**Nutrient Absorption:** The microbiome aids in the breakdown and absorption of nutrients, which are substrates for mitochondrial ATP production, influencing overall energy metabolism.

### Metabolic Regulation

**Insulin Sensitivity:** Certain gut bacteria help regulate blood glucose levels and improve insulin sensitivity, affecting metabolic pathways that involve mitochondrial function. Dysbiosis (microbial imbalance) has been linked to insulin resistance, which impacts mitochondrial efficiency.

### Inflammation and Oxidative Stress

**Gut Barrier Integrity:** A healthy microbiome supports the gut barrier, preventing the translocation of bacteria and toxins that can cause systemic inflammation. Inflammation is known to impair mitochondrial function.

**Antioxidant Production:** Some gut microbes contribute to the production of antioxidants that protect mitochondria from oxidative stress, which can damage mitochondrial DNA and impair ATP production.

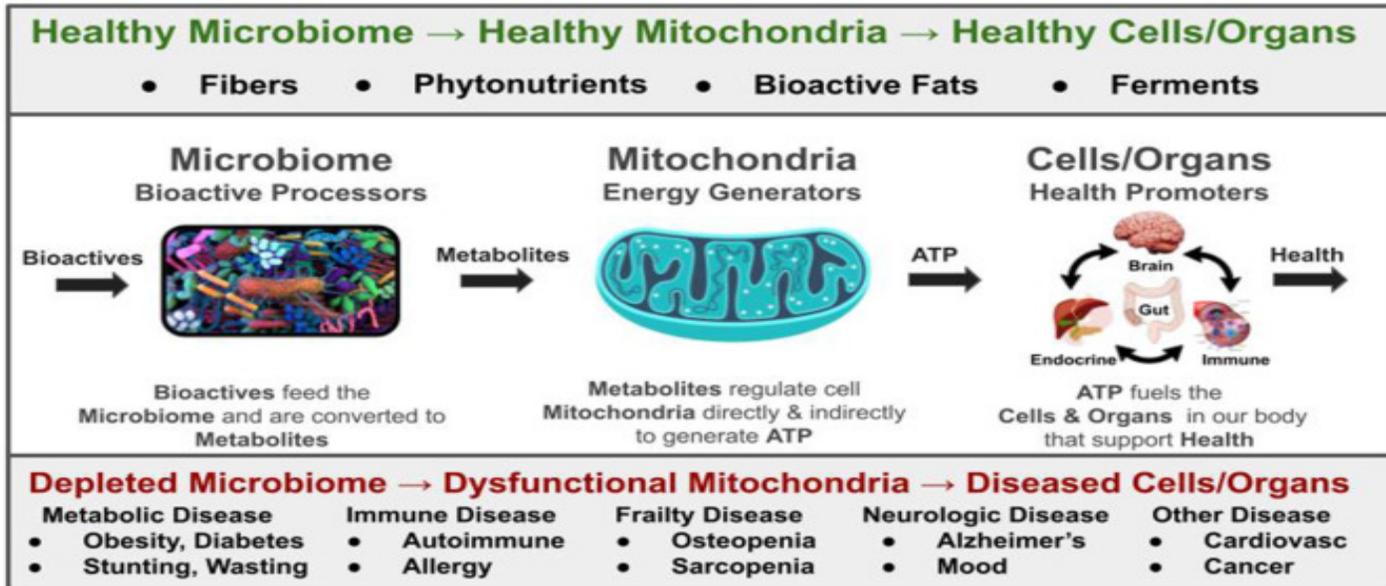
### Mitochondrial Biogenesis

**Signaling Pathways:** The microbiome can influence pathways that stimulate mitochondrial biogenesis, including the activation of AMPK and PGC-1 $\alpha$ , which are crucial for increasing mitochondrial mass and function.

## Gut-Brain Connection

**Neurotransmitter Production:** Gut bacteria can produce neurotransmitters (e.g., serotonin), which might influence mitochondrial function in neurons. This connection may play a role in neurodegenerative diseases.

## The Microbiome-Mitochondria Axis



## Implications for Health and Disease

**Metabolic Disorders:** An imbalance in the microbiome (dysbiosis) has been associated with conditions like obesity, type 2 diabetes, and metabolic syndrome, which are often linked to mitochondrial dysfunction.

**Chronic Diseases:** Mitochondrial dysfunction can lead to increased susceptibility to chronic diseases, including cardiovascular diseases, neurodegenerative disorders, and autoimmune conditions.

**Therapeutic Potential:** Modulating the microbiome through diet, pre and probiotics, is key to enhancing mitochondrial function and overall health.

The relationship between the microbiome and mitochondria is integral to maintaining metabolic homeostasis and overall health. An understanding of this connection underscores the importance of gut health in supporting mitochondrial function and can inform strategies for preventing and treating various health conditions through dietary and lifestyle interventions.

## Support

**Colicron Duo. Dose 1 Tablet AM. 1 Capsule PM.**

Colicron Duo is unique in that each box contains 15 tablets and 15 capsules. Each tablet contains **Berberine and Quercetin**. Each Capsule contains **Lactobacillus Rhamnosus GG, PEA, Undaria, and Hericium**.

One tablet is taken each morning and one capsule each evening.

The tablet containing Berberine and Quercetin offers a multifaceted approach to enhancing gut health, removing the “bad” bacteria while supporting the “good bacteria both are anti-inflammatory, and both strengthen the integrity of the gut lining reducing intestinal permeability (leaky gut) and improving gut barrier function.

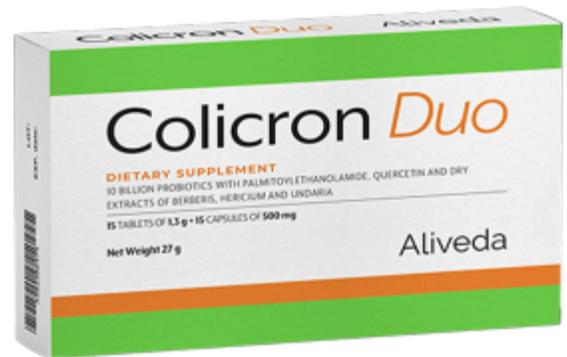
The Berberine Quercetin combination is key for mitochondrial function. By activating AMPK, Berberine improves your body’s ability to metabolize glucose (sugar) for energy and this is the main reason it is used for people with type 2 diabetes or metabolic syndrome.

The AMPK pathway also reduces cell proliferation.

Berberine affects DNA transcription (turning genes on or off), receptor expression (controlling the behavior of cells), and the interaction of other molecules with cells in your body, including antioxidants. As a powerful antioxidant, Quercetin helps combat oxidative stress in the gastrointestinal tract, protecting gut cells from damage and promoting overall gut health. Like Berberine Quercetin is antimicrobial and supports the integrity of the intestinal barrier

Berberine on its own is notoriously bad at getting out of the gut into systemic circulation. This is due to certain efflux transporters such as P-glycoprotein (P-gp.) which pump Berberine back into the gut as it tries to cross into systemic circulation. Quercetin has the ability to inhibit these transporters which increases the intracellular concentration of Berberine, prolongs the half-life of Berberine and allows Berberine into systemic circulation. Berberine although often touted for its efficacy with regards to metabolic syndrome, type 2 diabetes, and AMPK activation if taken in isolation is ineffective.

The Colicron *Duo* Capsule taken in the afternoon or evening contains Lactobacillus Rhamnosus GG, PEA, Undaria, and Hericium. Together these ingredients offer Pre, Pro and Post biotic support replenishing the microbiome and offering anti-inflammatory support.



## Additional Support Considerations

### **DR. Magnesium Complex.**

Insufficient magnesium leads to dysfunction in energy production, cellular health and performance

### **DR. Turmeric Boswellia C.**

A combination to reduce oxidative stress and is anti-inflammatory.

### **DR. Wheat Germ Oil E.**

An antioxidant that helps protect mitochondrial membranes from oxidative damage.

### **PRL. Green Tea ND.**

Contains catechins that act as antioxidants, promoting mitochondrial health and function.

### **PRL. Curcumin FX.**

Anti-inflammatory properties enhance mitochondrial function and reduce oxidative stress.

### **PRL. Premier Ashwagandha.**

Supports through antioxidant properties, anti-inflammatory effects, stimulation of mitochondrial biogenesis, and adaptation to stress