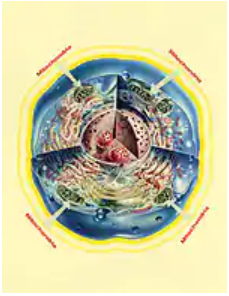
Life Extension Magazine®

Rejuvenate Your Cells by Growing New Mitochondria

Aged people suffer up to **95% damaged** mitochondria compared to almost none in a 5-year old. To combat the horrific effects of ***mitochondrial insufficiency,*** from cancer to heart failure, it is critical to maintain youthful mitochondrial function and structure. In an unprecedented advance, a nutrient called **PQQ** triggers **mitochondrial biogenesis**—the growth of new mitochondria in aging cells!

Scientifically reviewed by: **Dr. Gary Gonzalez**, MD, in January 2021. Written by: Kirk Stokel.

Mitochondrial dysfunction is a primary cause of age-related decline.[1-7] In a revealing study, a team of researchers showed that muscle tissue of a 90-year-old man contained 95% damaged mitochondria compared to almost no damage in that of a 5-year-old.[8]



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When one looks at the boundless energy of a child compared to an elderly person, the devastating impact of *mitochondrial degradation* become instantly apparent. A myriad of recent scientific reports link defective and deficient ***mitochondria*** to virtually all degenerative diseases including Alzheimer's, type 2 diabetes, heart failure, and cancer.[9-13]

Up until now, the best we could do was protect and improve the ***function*** of existing mitochondria using nutrients like **L-carnitine, lipoic acid,** and **coenzyme Q10.**

In an unprecedented breakthrough, a compound has been discovered that promotes the growth of new mitochondria structures within aging cells![14]

In this article, you will discover how this novel compound can help reverse cellular aging by activating genes that stimulate ***mitochondrial biogenesis,*** which means **the generation of new mitochondria.**

*The more **functional** mitochondria you have in your **cells,** the greater your **overall health** and **durability.***

Mitochondria are the only cell components (other than the nucleus) to possess their own DNA. This means mitochondria have the ability to replicate and increase their number within a single human cell.

Human cells may house anywhere from **2** to **2,500** mitochondria,[15-17] depending on tissue type, antioxidant status, and other factors.

A growing number of biologists espouse the theory that mitochondrial number and function ***determine human longevity.***[18-20] To put it simply, the more functional mitochondria you have in your cells, the greater your overall health and durability.

The problem is that as we age, our mitochondria degrade and become dysfunctional. Age-related destruction of the mitochondria occurs more rapidly than in other cell components, meaning that for most people it is loss of *functional* mitochondria that ultimately leads to personal extinction.

The challenge aging humans face is that methods to increase the generation of new mitochondria are difficult to achieve. Up until recently, the only natural ways to stimulate mitochondrial *biogenesis* were **calorie restriction or exhaustive physical activity.**

A natural agent with the power to safely induce ***mitochondrial biogenesis*** would mark an extraordinary advance in the quest to halt and reverse cellular aging. A compound called ***pyrroloquinoline quinone*** or **PQQ** is *rapidly emerging as that nutrient.*

WHAT YOU NEED TO KNOW

The rate of aging affects the number of mitochondria we have in our cells. CoQ10 is well-known for its ability to enhance mitochondrial function, however new research is showing the importance of PQQ for its ability to protect and create new mitochondria.

PQQ: A Quantum Leap That May Reverse Cellular Aging

PQQ (*pyrroloquinoline quinone*) plays a critical role across a range of basic life functions. As an ultra potent antioxidant, it provides extraordinary defense against mitochondrial decay: PQQ's chemical structure enables it to withstand exposure to oxidation up to 5,000 times greater than **vitamin C.**[21]

When combined with **CoQ10,** research shows just **20 mg per day** of **PQQ** can significantly preserve and enhance memory, attention, and cognition in aging humans.[22]

But the most exciting revelation on **PQQ** emerged early in **2010,** when researchers found it not only protected mitochondria from oxidative damage—it also stimulated **growth of *new* mitochondria!**[14]

PQQ Is an Essential Micronutrient

PQQ is ubiquitous in the natural world. It has been found in all plant species tested and is present in human milk. Humans, however, are not capable of synthesizing it.[23] This has led researchers to classify PQQ as an **essential micronutrient.**

PQQ's potential to stimulate ***mitochondrial biogenesis*** was foreshadowed by early findings indicating its central role in growth and development across multiple forms of life.

PQQ has been shown to be a potent growth factor in plants, bacteria, and higher organisms.[21,24,25] Pre-clinical studies reveal that when deprived of dietary PQQ, animals exhibit stunted growth, compromised immunity, impaired reproductive capability, and most importantly, ***fewer mitochondria in their tissue.*** Rates of conception, the number of offspring, and survival rates in juvenile animals are also significantly reduced in the absence of PQQ.[26-28]

When PQQ is introduced back into the diet, it reverses these effects, restoring systemic function while simultaneously *increasing* mitochondrial number and energy efficiency.

These compelling data prompted a team of researchers at the **University of California-Davis** to specifically analyze PQQ's influence on cell signaling pathways involved in the formation of new mitochondria.[14]

Their work, published last year, led to several extraordinary discoveries. They found that PQQ's critical biological roles stem from its ability to activate **genes** directly involved in cellular energy metabolism, development, and function.[14]

Their findings shed light on results from favorable prior studies. For example, PQQ deficiency in juvenile mice results in a **20-30%** reduction in the number of mitochondria in the liver, elevated blood glucose, and impairment in oxygen metabolism.[26] These are hallmark indicators of ***mitochondrial dysfunction.*** Yet when PQQ was put back into the diet, these pathological effects were reversed, along with an increase observed of new mitochondria.

These and additional animal model data[28] taken together confirm PQQ's ability to significantly boost mitochondrial number and function—a key to cellular anti-aging and longevity.

The sidebar on the below reveals the complex mechanisms by which PQQ activates genes that stimulate ***mitochondrial biogenesis.***

Protecting Against Mitochondria-generated Free Radicals

As the primary energy engines of our cells, the mitochondria rank among the structures *most* vulnerable to destruction from *oxidative* damage.

The formidable free radical-scavenging capacity of PQQ furnishes the mitochondria considerable antioxidant protection.

At the core of this capacity is an extraordinary molecular **stability.**[35] As a bioactive coenzyme, PQQ *actively* participates in the energy transfer within the mitochondria that supplies the body with most of its bioenergy (like **CoQ10**).

Unlike other antioxidant compounds, the **stability** of PQQ allows it to carry out thousands of electron transfers *without* undergoing molecular breakdown. It has been proven especially effective in neutralizing the ubiquitous ***superoxide*** and ***hydroxyl*** radicals.[36] According to the most recent research, "PQQ is **30 to 5,000 times** more efficient in sustaining redox cycling . . . than other common [antioxidant compounds], e.g. ascorbic acid."[37]

Protection Against Brain Aging

PQQ has been shown to optimize function of the entire central nervous system. It *reverses* cognitive impairment caused by chronic oxidative stress in pre-clinical models, improving performance on memory tests.[40] It has also been shown to safeguard a gene involved in the development of Parkinson's disease (called DJ-1) from *self-oxidation*—an early step in the onset of Parkinson's.[41]

Reactive *nitrogen* species (RNS), like reactive *oxygen* species, impose severe stresses on damaged neurons.[42] They arise spontaneously following stroke and spinal cord injuries and have been shown to account for a substantial proportion of subsequent long-term neurological damage. PQQ directly *suppresses* RNS in experimentally induced strokes.[43] It also provides additional protection by blocking gene expression of *inducible* nitric oxide synthase, a major source of RNS, following spinal cord injury.[44]

PQQ protects brain cells against damage following ***ischemia-reperfusion injury***—the inflammation and oxidative damage that result from the sudden return of blood and nutrients tissues deprived of them by stroke.[45] Given immediately before induction of stroke in animal models, PQQ significantly reduces the size of the damaged brain area.[46] This finding implies that if a person were to suffer a temporary loss of cerebral blood flow due to cardiac arrest, stroke, or trauma, that having PQQ in their body would afford considerable protection against permanent brain damage.

PQQ also beneficially interacts with brain neurotransmitter systems. In particular, PQQ protects neurons by modifying the important NMDA receptor site.[47,48] NMDA is a powerful mediator of "excitotoxicity," a response to long-term overstimulation of neurons that is associated with many neurodegenerative diseases and seizures.[49-51] PQQ protects against neurotoxicity induced by other toxins, including **mercury.**[52,53]

A mounting body of evidence points to PQQ as a potent intervention in **Alzheimer's** and **Parkinson's disease.** Both are triggered by accumulation of abnormal proteins that initiate a cascade of oxidative events resulting in brain cell ath.

HOW PQQ GENERATES NEW MITOCHONDRIA

Mitochondrial biogenesis can be defined as the growth and division of pre-existing mitochondria. This

phenomenon is not only accompanied by increased mitochondria numbers, but also their size and mass.

Mitochondrial biogenesis requires the *coordinated* synthesis and import of 1,000-1,500 proteins where they facilitate the production of healthy new mitochondria.

Mitochondrial biogenesis occurs through the combined effects of **genes** activated by **PQQ** via the following three mechanisms:

- **PQQ** increases expression of peroxisome proliferator-activated receptor gamma coactivator 1-alpha or **PGC-1**α. PGC-1α is a "master regulator" gene that mobilizes your cells' response to various external triggers. It directly activates genes that boost mitochondrial and cellular respiration, growth, and reproduction. Its capacity to modulate cellular metabolism at the genetic level favorably affects **blood pressure, cholesterol** and **triglyceride** breakdown, and the onset of **obesity.**[29]
- **PQQ** activates a signaling protein known as cAMP-response element-binding protein or **CREB.** The CREB gene plays a pivotal role in embryonic development and growth. It also beneficially interacts with histones, molecular compounds shown to protect and repair cellular DNA. CREB *also* stimulates the growth of new mitochondria.[30]
- **PQQ** regulates a recently discovered gene called **DJ-1.** As with PGC-1α and CREB, DJ-1 is intrinsically involved in cell function and survival. It has been shown to **prevent cell death** by combating intensive antioxidant stress and is of particular importance to brain health and function. DJ-1 damage and mutation have been conclusively linked to the onset of **Parkinson's disease** and other neurological disorders.[31-34]

PQQ prevents development of *alpha-synuclein,* the protein responsible for Parkinson's disease.[54] It also protects nerve cells from the oxidizing ravages of the Alzheimer's-causing amyloid-beta protein.[55] A **2010** study revealed that PQQ could prevent formation of amyloid-beta molecular structures.[56] These effects were traced to three distinct biochemical mechanisms described in the sidebar above.

PQQ has also been shown to protect memory and cognition in aging animals and humans.[22,57] It stimulates production and release of nerve growth factor in cells that support neurons in the brain.[58] This may partially explain why PQQ supplementation of aging rats resulted in marked retention of their maximum memory function.[57]

In humans, supplementation with **20 mg per day** of PQQ resulted in improvements on tests of higher cognitive function in a group of middle-aged and elderly people.[22] These effects were significantly amplified when the subjects also took **300 mg** per day of **CoQ10.** Presumably a lower dose of the more *absorbable* **ubiquinol** form of CoQ10 would provide the same benefit as **300 mg** of **ubiquinone.**

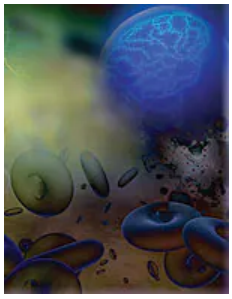
***PQQ** has also been shown to protect **memory** and **cognition** in both aging animals and **humans**.*

Cardiovascular Defense

As with strokes, damage in heart attacks is inflicted via ***ischemia-reperfusion*** injury. Ischemia-reperfusion means loss of blood flow (ischemia) to part of the body and the subsequent re-flow (reperfusion) when blood flow is restored. Cells are injured when blood flow is interrupted and often sustain even greater damage when blood flow is suddenly restored.

Supplementation with PQQ reduces the size of ischemia-reperfusion damaged areas in animal models of acute myocardial infarction (heart attack).[59] This occurs whether the supplement is en before or after the ischemic event itself.

further investigate this potential, researchers at the VA Medical Center at UC-San Francisco mpared PQQ with **metoprolol,** a commonly prescribed beta blocker that is standard post-heart attack clinical treatment.[60] Given alone, both treatments reduced the damaged areas' size



and protected against heart muscle dysfunction. When they were given together, the left ventricle's pumping pressure was enhanced. The combination also increased mitochondrial **energy-producing** functions—but the effect was small compared with the better response seen with PQQ alone![60] And only PQQ favorably reduced lipid peroxidation. The remarkable conclusion: ***"PQQ is superior to metoprolol in protecting mitochondria from ischemia/reperfusion oxidative damage."***[60]

Subsequent research from the same team has demonstrated that PQQ helps heart muscle cells resist acute oxidative stress.[61] The mechanism? *Preserving and enhancing mitochondrial function.*

WHY MITOCHONDRIA ARE SO VULNERABLE TO FREE RADICAL DAMAGE

The death spiral of our mitochondria is accelerated by the very physiological function they must perform, i.e. energy production.

As the cell's power generators, mitochondria are the site of enormous and constant *oxidative* activity that spews out toxic **free radicals.** To make matters worse, relative to nuclear DNA, ***mitochondrial DNA possesses few defenses against free radical damage.***[38,39]

DNA in the cell's nucleus is protected by numerous "guardian" proteins that blunt the impact of free radicals. No such repair systems exist to protect mitochondrial DNA.

Nuclear DNA also enjoys superior structural defenses. It is housed within a protective double-membrane that separates it from the rest of the cell. This double-membrane is complemented by a dense matrix of filament proteins called the *nuclear lamina,* a kind of hard shell casing to further buffer DNA from external impacts.

By comparison, **mitochondrial DNA** is left almost entirely exposed: it attaches *directly* to the inner membrane where the mitochondria's electrochemical furnace rages continuously, generating an enormous volume of toxic reactive oxygen species. This is why supplementation with **lipoic acid, carnosine,** and other mitochondrial-protecting antioxidants is so important.

The extraordinary antioxidant capacity of **PQQ** represents a powerful new intervention that may effectively reinforce the mitochondria's meager defenses.

Summary

Cellular aging is intimately associated with the decline in mitochondrial number and functionality. Nutrients that provide protection to existing mitochondria include resveratrol, carnosine, lipoic acid, L-carnitine, and CoQ10.

During the course of normal aging, however, the number of *functional* mitochondria pathologically diminishes, leading to a host of debilitating disorders followed by death of the organism.

For the first time in scientific history, a natural compound called **PQQ** is available to increase the functionality of existing mitochondria while promoting the generation of new mitochondria inside aging cells.

If you have questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

Editor's Note

ence continues to evolve, and new research is published daily. As such, we have a more recent article on this ic: **How PQQ Slows Aging**

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