REPORT

Powerful Protection Against Cellular Aging

By Michael Downey

Conclusive evidence now indicates that PQQ (pyrroloquinoline quinone) activates cell signaling pathways that have the potential to reverse cellular aging!

PQQ has previously been shown to promote growth of new mitochondria within aging cells,1–3 up-regulate cellular metabolism,1,2 protect neurons,4–7 and repair DNA!1,8

These and other synergistic signaling effects have the combined ability to promote longevity at the critical subcellular level.

PQQ has been found in all plant species ever tested. Scientists have gone so far as to state that PQQ may be "vital to life."3

AN ESSENTIAL ANTI-AGING NUTRIENT

Scientists have found that PQQ, a critical coenzyme, plays a leading role in boosting critical cell signaling mechanisms.3

These signaling pathways regulate a variety of physiological and molecular processes throughout the body—processes that have an impact on key biomarkers of aging, such as mitochondrial function11–16 and cellular defense against oxidative stress.10

Through these effects, the cell signaling power of PQQ targets aging at both the cellular and subcellular levels.

New research confirm that humans can obtain these multiple benefits after even just short-term supplementation.17

A wealth of studies now confirm that PQQ's cell-signaling activity translates into substantial protection against degenerative and age-related conditions, such as mitochondrial dysfunction,1 heart degeneration,18–20 brain injury, and cognitive decline.21–40 As one example, research shows that 20 mg of PQQ daily may reverse age-related cognitive decline in aging humans!

Since PQQ cannot be synthesized by your body it is necessary to obtain PQQ from outside sources.24,41–43 Fortunately, compared to other plant compounds, PQQ has greater solubility and bioavailability. PQQ is water-soluble and therefore, more easily absorbed at low supplemental intakes.1,44,45

Let's take a look at the modes of action behind PQQ's multiple effects.

PQQ AND CELL SIGNALING

How can PQQ target multiple aging factors?

The answer lies in the potent and unique capacity of PQQ to activate cell signaling pathways, especially those directly involved in cellular energy metabolism.
Also, similar to the action of CoQ10, PQQ actively participates in the energy transfer within the mitochondria that supplies the body with most of its bioenergy.

PQQ can even trigger spontaneous mitochondrial biogenesis—the creation of fresh, new mitochondria!

Specific cell signaling molecules have been found to be directly activated by PQQ.

CELL SIGNALING PATHWAYS

Early studies revealed that animals deprived of PQQ exhibit signs of accelerated aging in the form of elevated plasma glucose concentrations, impaired oxygen metabolism, stunted growth, compromised immunity, impaired reproductive capability, reduced numbers and survival rate of offspring, and a decrease in energy-producing mitochondria in their tissue. Reintroducing PQQ to their diet reversed these effects, increasing mitochondrial numbers and restoring systemic function.46-48

PQQ is now linked to favorable effects on cell development, metabolism, and mitochondrial biogenesis. It provides the potential to reverse cellular aging and age-related disease by:

- Stimulating spontaneous growth of new mitochondria within aging cells.1
- Regulating gene expression.3
- Promoting tumor cell death from apoptosis.49
- Supporting mitochondrial protection and repair.1
- Providing powerful antioxidant support to mitochondria and other body molecules—with up to 5,000 times the effect of other antioxidants,4 and protecting the brain's cells and neurotransmitter systems against neurotoxicity5,39,50 and amyloid-beta protein.36

The end result of PQQ's activity is subcellular anti-aging and enhanced longevity.

(For more on these beneficial pathways, see previous box titled, 'PQQ and Cell Signaling.')

HEART BENEFITS

PQQ's cell signaling activities produce measurable health improvements, especially cardio-protective and neuro-protective benefits.

For example, research with animals found that supplementation with PQQ decreased the size of the area of the heart injured by acute coronary artery blockage. This protective effect was found whether PQQ was given before or after the event—suggesting taking PQQ within the first hours following a cardiac event could deliver invaluable benefit to patients.18

Following up on this research, scientists then tested both PQQ and the common post-heart-attack treatment metoprolol (Lopressor®). They found that, while both reduced the size of the damaged area, there was a greater increase in mitochondrial energy-producing functions with PQQ.

And only PQQ lowered lipid peroxidation!

The study team concluded that "PQQ is superior to metoprolol in protecting mitochondria from ischemia/reperfusion oxidative damage."19

These same scientists found in later animal research, that "PQQ reduces oxidative stress, mitochondrial dysfunction, and cell death" in cardiac muscle cells.20

What You Need to Know

PQQ: POWERFUL PROTECTION AGAINST CELLULAR AGING
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**BRAIN EFFECTS**

Scientists found in pre-clinical trials that PQQ reversed cognitive impairment caused by oxidative stress and improved performance on memory tests. PQQ was shown to protect against a pathologic gene protein associated with Parkinson's disease. Much of the long-term neurological damage that arises after a stroke or spinal cord injury is caused by reactive nitrogen species which impose severe stresses on damaged neurons. However, PQQ was found to suppress reactive nitrogen species in induced strokes.

PQQ also blocked a source of reactive nitrogen species following spinal cord injury. Researchers concluded that PQQ significantly reduces the size of the damaged area of the brain even if administered 3 hours after the stroke. Additionally, it provides potent protection against the inflammation and oxidative damage that results from the sudden return of blood and nutrients to tissues deprived of them by stroke. It would seem that PQQ should become a standard nutrient in the hospital emergency room setting for rapid administration to stroke victims.

**PQQ AND MITOCHONDRIAL BIOGENESIS**

Greater mitochondrial damage has been found in brain cells of humans over 70 relative to those in their early 40s. Many scientists believe mitochondrial longevity and the number of functioning mitochondria determine overall human longevity. The coenzyme PQQ, has been shown to induce mitochondrial biogenesis—the growth of new mitochondria in aging cells.

While coenzyme Q10, or CoQ10, optimizes the function of mitochondria, PQQ activates genes that govern mitochondrial reproduction, protection, and repair.

To date, the only ways known to reliably stimulate mitochondrial biogenesis have been sustained calorie restriction or strenuous physical activity—potentially too rigorous for aging individuals.
With its power to safely trigger mitochondrial biogenesis, PQQ represents an extraordinary advance in the quest to reverse cellular aging. 

Illustrating its cell signaling mechanism, PQQ protects neurons by modifying a key receptor site within our brain's neurotransmitter system. This inhibits excitotoxicity, a response to long-term over-stimulation of neurons that is associated with many neurodegenerative diseases and seizures. PQQ was shown to block neurotoxicity induced by other toxins, including mercury, a factor suspected to play a role in the development of Alzheimer's disease.

Accumulating research indicates that PQQ serves as an intervention in Alzheimer's and Parkinson's disease—blocking development, and oxidative effects, of both the amyloid beta protein associated with Alzheimer's and the alpha-synuclein protein associated with Parkinson's, before they can cause damage. PQQ has been observed to deliver substantial cognitive benefits, including improved memory and attention. It activates the manufacture and release of an important, neuro-protective, nerve growth factor. Scientists tested PQQ's cognitive effects in a double-blind, placebo-controlled clinical trial conducted on humans. In this study of healthy individuals ranging from 45 to 65 years of age, 20 mg a day of PQQ produced clear improvements on standard tests of greater cognitive function. Also, the PQQ test group scored two-fold higher on memory tests than the control group.

Scores were dramatically higher for a third group that received 300 mg per day of CoQ10 along with their 20 mg of PQQ. This underscores the powerful cognitive benefits of supplementation with agents shown to be involved in mitochondrial energy production.

PQQ AND GENE EXPRESSION

Recent rodent research on gene expression has shown that an induced deficiency of the coenzyme pyrroloquinoline quinone, or PQQ, results in an altering of the expression of a total of 438 genes. When the diet is then supplemented with PQQ, the genetic expression pattern reverts to normal. On investigation, the genes most affected by PQQ turned out to be those responsible for:

- Cell signaling
- Cellular stress
- Growth of new mitochondria
- MAP kinase pathways (cell-surface-to-nucleus signaling proteins)
- Transport of metabolites

These findings shed light on PQQ's genetic involvement with cell signaling, antioxidant activity, and mitochondrial biogenesis.

SUMMARY

Through its broad cell signaling activity, PQQ (pyrroloquinoline quinone) modulates the many pathways of aging!

Scientific findings indicate that PQQ-enhanced signaling stimulates mitochondrial biogenesis, boosts cellular metabolism, improves cognitive performance and protects neurotransmitters, and repairs DNA.

Together, these mechanisms support subcellular anti-aging and promote longevity.

Studies have shown that PQQ beneficially modulates biomolecular functions that result in substantial heart and brain defense. As one example, scientists found that PQQ helped produce remarkable reversal of cognitive decline in aging humans.

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

PROTECTING MITOCHONDRIAL DNA
Degradation of mitochondrial DNA leads to mitochondria senescence and death—and extinction of the "host" organism.

As the power generators responsible for almost all bioenergetic production, mitochondria are the site of enormous oxidative activity. A nearly incalculable number of electrons are constantly flowing within the mitochondria, throwing off an equally enormous number of free radicals.

As a result, **mitochondria are much more vulnerable to biochemical insults** than other cellular structures.

And as scientists have discovered over the past several decades, mitochondrial DNA—relative to genetic DNA in the cell's nucleus (nuclear DNA)—possesses few defenses against free radical damage.\(^{55,56}\)

Nuclear DNA is protected by numerous guardian proteins—histones and repair enzymes—that blunt the impact of free radicals. Similar repair systems do not exist to protect mitochondrial DNA.\(^{55-57}\)

Also, nuclear DNA 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 is attached directly to the inner membrane where the mitochondria's electrochemical furnace rages continuously, generating an enormous volume of toxic reactive oxygen species.

The mitochondria rank among the physiological structures most vulnerable to destruction from oxidative damage.

And scientific studies link genetic mutation within the mitochondria to human aging.\(^{57-59}\)

**PQQ's formidable free radical-scavenging capacity furnishes the mitochondria with superior antioxidant protection.**

As a bioactive coenzyme, PQQ supports optimal function within the mitochondria which is responsible for supplying the body with most of its bioenergy.\(^{60}\)

Unlike other antioxidant compounds, PQQ's ex-ceptional stability allows it to carry out *thousands* of these electron transfers without undergoing molecular breakdown.

In fact, **PQQ is up to 5,000 times more efficient in sustaining antioxidant capacity** than other common antioxidant compounds, such as ascorbic acid.\(^4\)


