

# ***Enhancing Mitochondrial Function***

With a Focus on the Importance of PQQ

# ***AGENDA***

- What are mitochondria?
- Mitochondria and aging.
- Health conditions linked to impaired mitochondrial function.
- Nutrients to enhance mitochondria.
- Pyrroloquinoline quinone (PQQ).
- Questions and answers.

# Theories of Aging:

- Oxidative Damage
- Telomere Shortening
- **Mitochondrial Aging**

# Mitochondria and Aging

- Damage to mitochondrial genome!
- Impaired mitochondrial gene expression.
- Inability of mitochondria to replicate, divide, further reducing energy production, etc.
- Damaged mitochondria replicate faster than intact mitochondria.

# Factors that Promote Mitochondrial Aging

- **Lifestyle**
- **Attitude**
- **Diet**
- **Environment**

# ***What health conditions are linked to impaired mitochondrial function?***

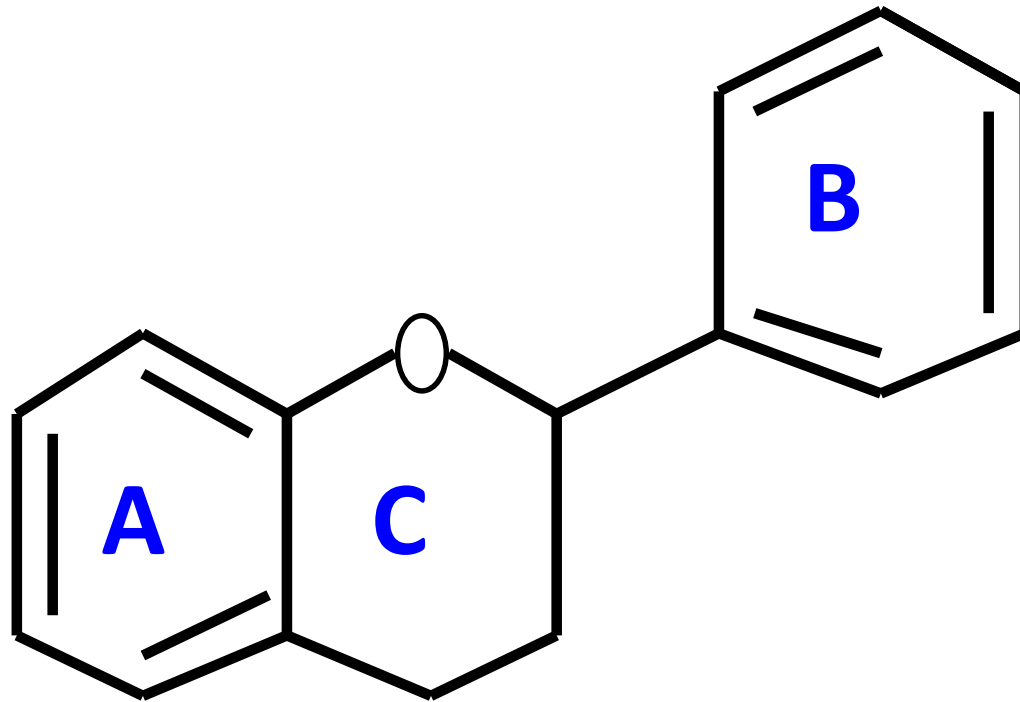
## **Key areas of focus:**

- Mitochondrial diseases
- Aging and degenerative disorders
  - Neurodegenerative disease
  - Cancer
- Autoimmune disorders
- Chronic fatigue syndrome
- Brain disorders:
  - Anxiety
  - Attention deficit disorder
  - Autism
  - Depression

# How do you improve mitochondrial function?

- A four-part strategy is required:
  - Provide essential nutrients
  - Provide protection from oxidative damage
  - Enhance detoxification processes
  - Reduce other damaging factors
    - Environmental toxins
    - Drugs (Rx and illicit)
    - Insulin resistance

# ***Basic Flavonoid Structure***



Over 4,000 flavonoids have been chemically classified.



# Flavonoids:

## Nature's Biological Response Modifiers

### Pharmacological Actions:

- Antioxidant
- Anti-allergy
- Anti-inflammatory
- Antiviral
- Antineoplastic

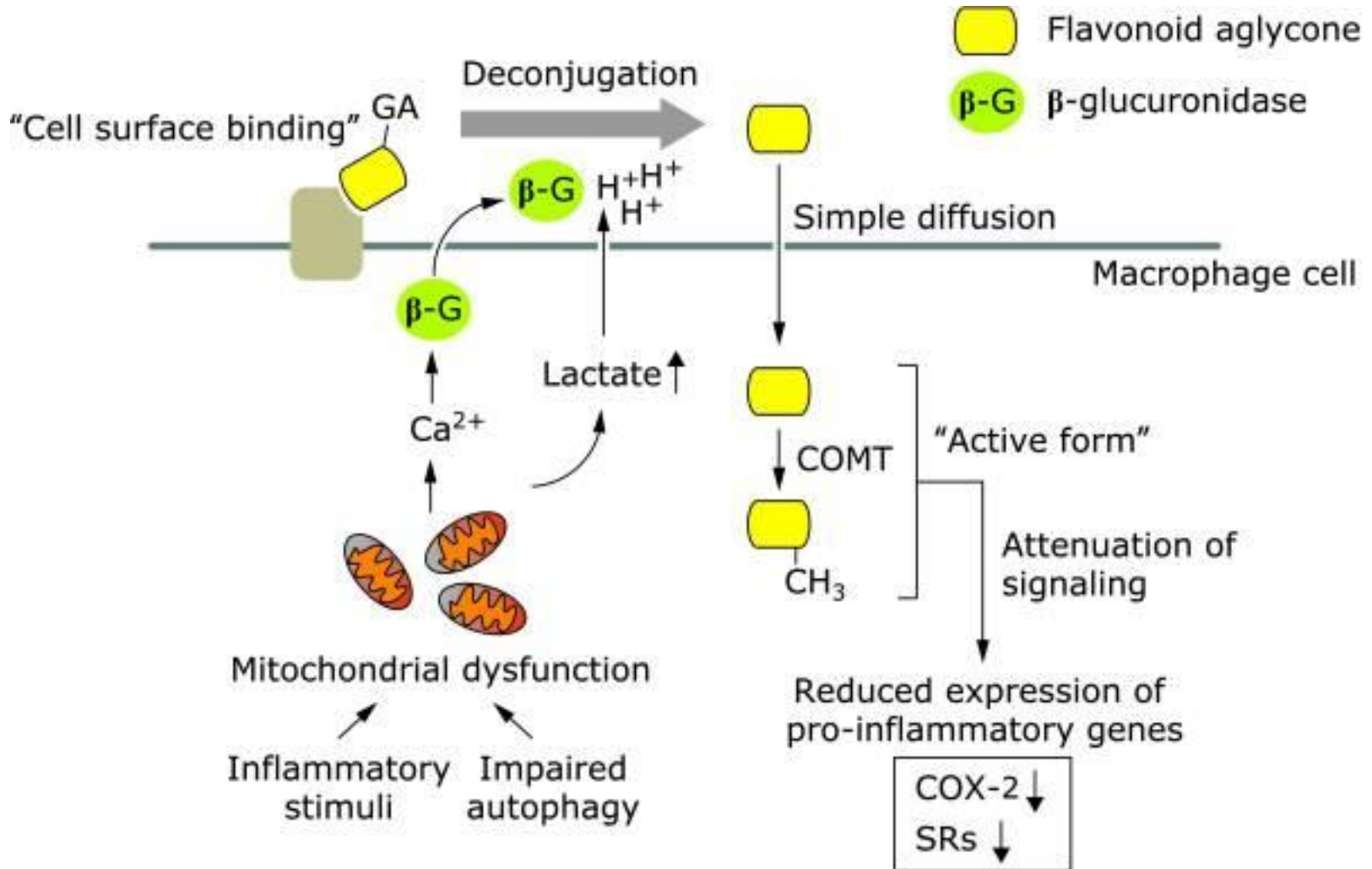
# *Flavonoid-Rich Extracts:*

## *Tissue Specific Antioxidants*

### Examples:

- *Quercetin/EMIQ* – Mast cells; best for allergies and eczema.
- *Bilberry* or *Blueberry extract* (*anthocyanosides*) – Retina; best for eyes.
- *Grapeseed extract* (*procyanidolic oligomers*) – LDL cholesterol, retina, vascular lining, lungs; best overall antioxidant.
- *Milk thistle extract* (*silymarin*) – Liver and breast.
- *Hawthorn* (*procyanidins*) and *Hibiscus* (*anthocyanins*) – Heart, aorta, arteries; best for heart disease.
- *Green tea* (*polyphenols*) – Weight loss promotion, LDL cholesterol, gastrointestinal tract; best for cancer prevention.
- *Ginkgo biloba* (*ginkgo flavonglycosides*) – Brain, vascular lining; often best choice for people over 50 years of age.

# Deglucuronidation at Sites of Need

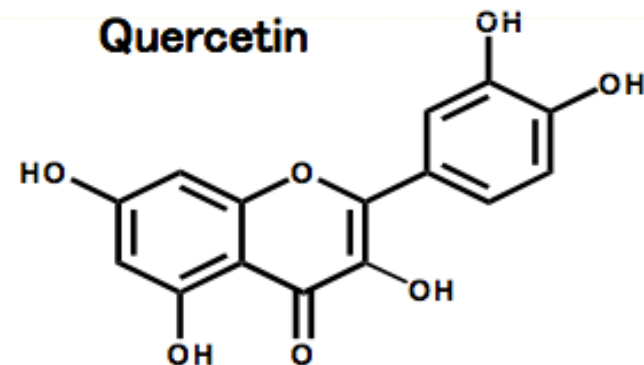
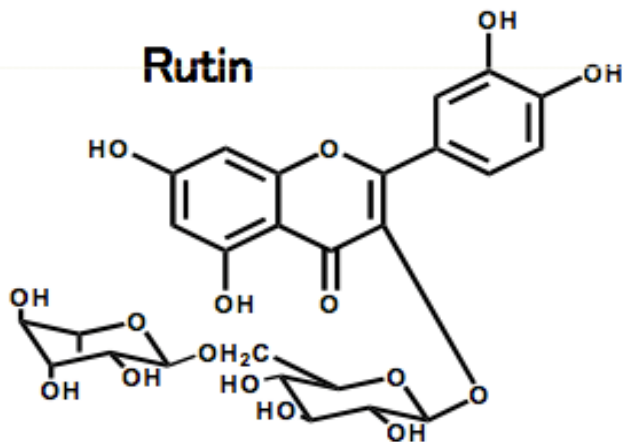
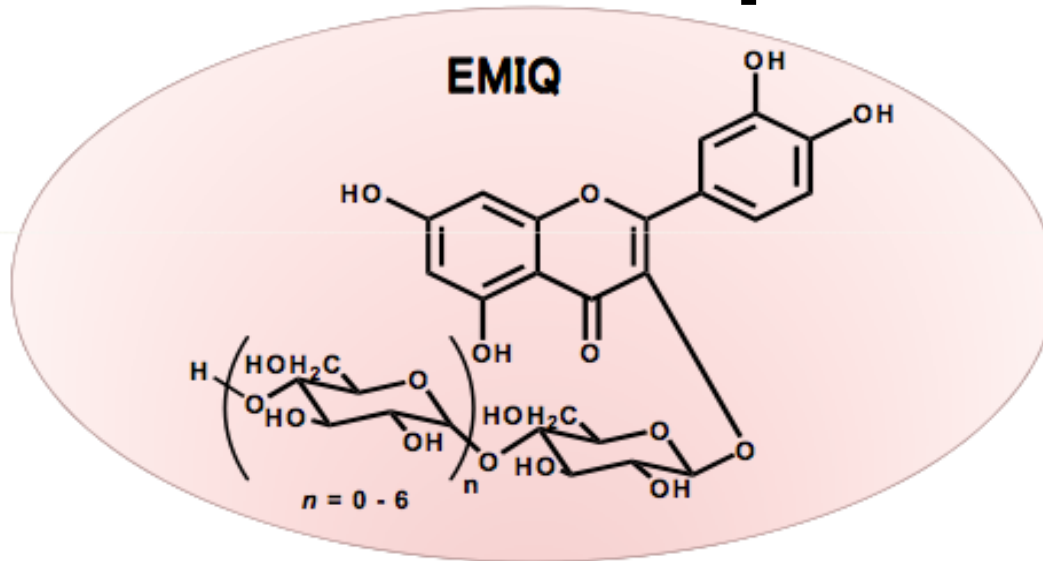


# Quercetin and Athletic Performance

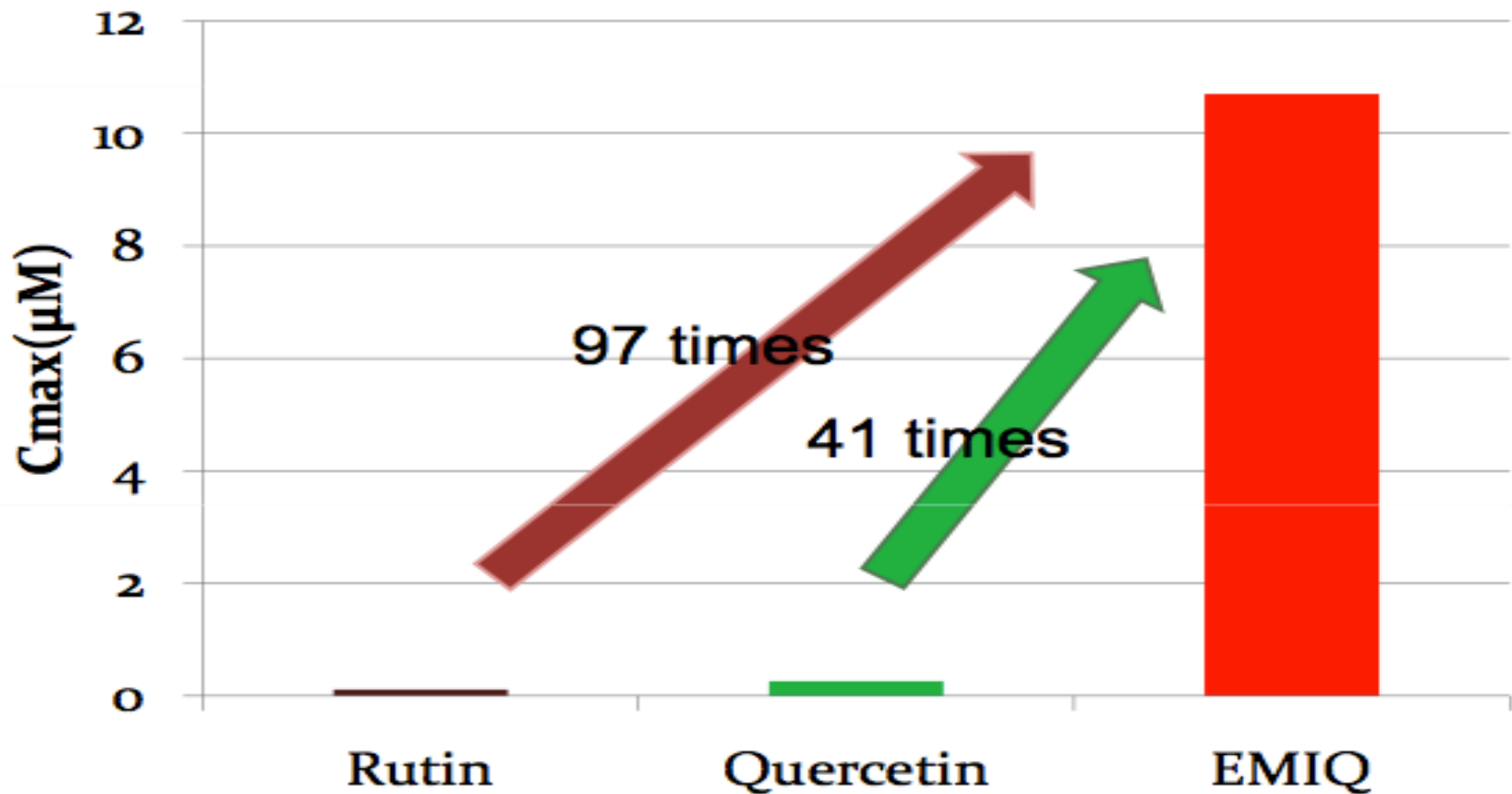
## *Results from double-blind studies*

- Quercetin at dosages of 1 g/day:
  - Increases net distance in a 12 min. treadmill by 2.9%
  - In cyclists, increase in VO<sub>2</sub>max (3.9%) along with a substantial (13.2%) increase in ride time to fatigue
  - Increases skeletal muscle messenger RNA expression (range = 16-25%) for sirtuin 1 and other markers
  - Reduces upper respiratory infections in moderately trained individuals - only 1/20 developed symptoms in the quercetin group compared to 9/20 in the placebo group

# Enzymatically Modified Isoquercitrin



# EMIQ Effectively Increases Serum Quercetin Metabolite Levels

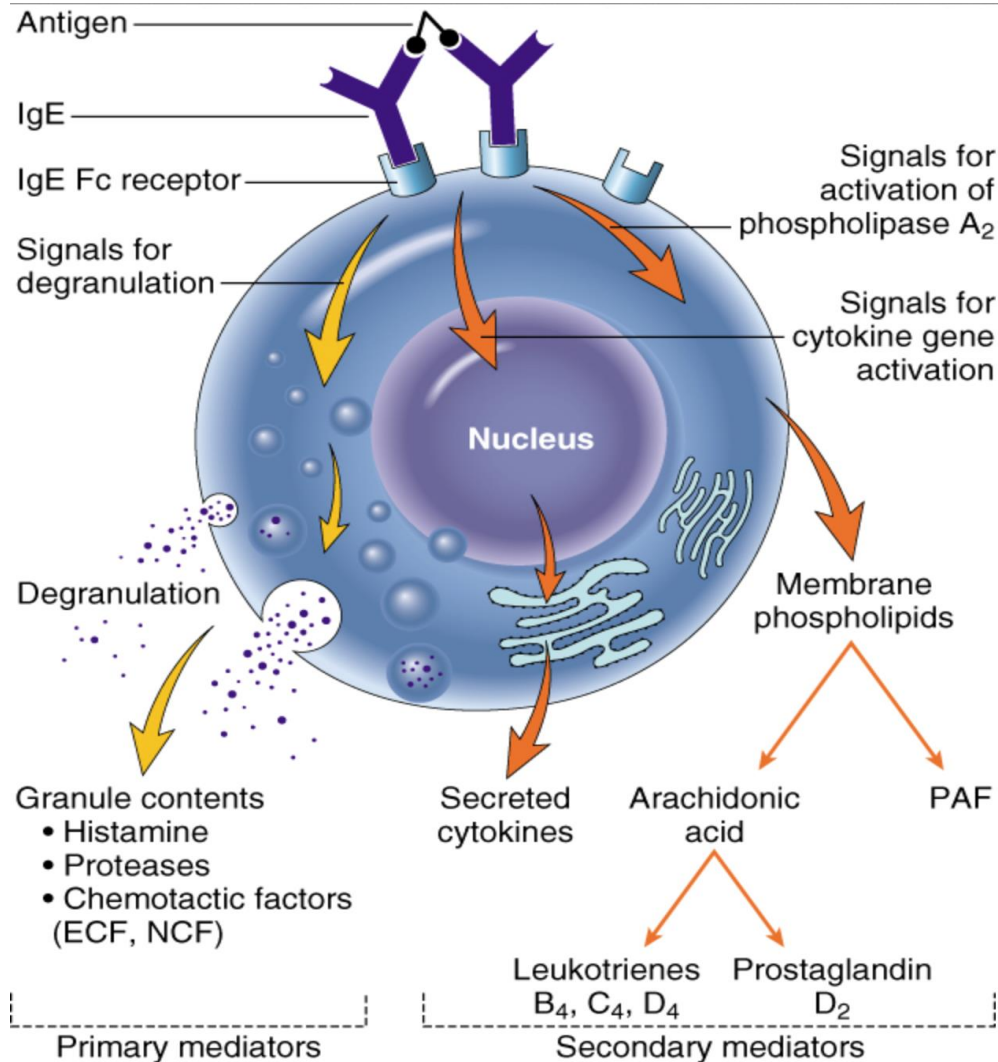


# EMIQ in Hayfever

*Double-blind, placebo-controlled study 1*

During the entire 8 week study period, total ocular score and ocular itching score for the EMIQ group were significantly lower than for the placebo group. When limited to the periods of pollen release, total symptom score for the EMIQ group was significantly lower than that for the placebo group. EMIQ reduced oxidized LDL; and thymus- and activation-regulated chemokine.

# Quercetin Exerts Significant Anti-Allergy Effects





# **EMIQ in Hayfever**

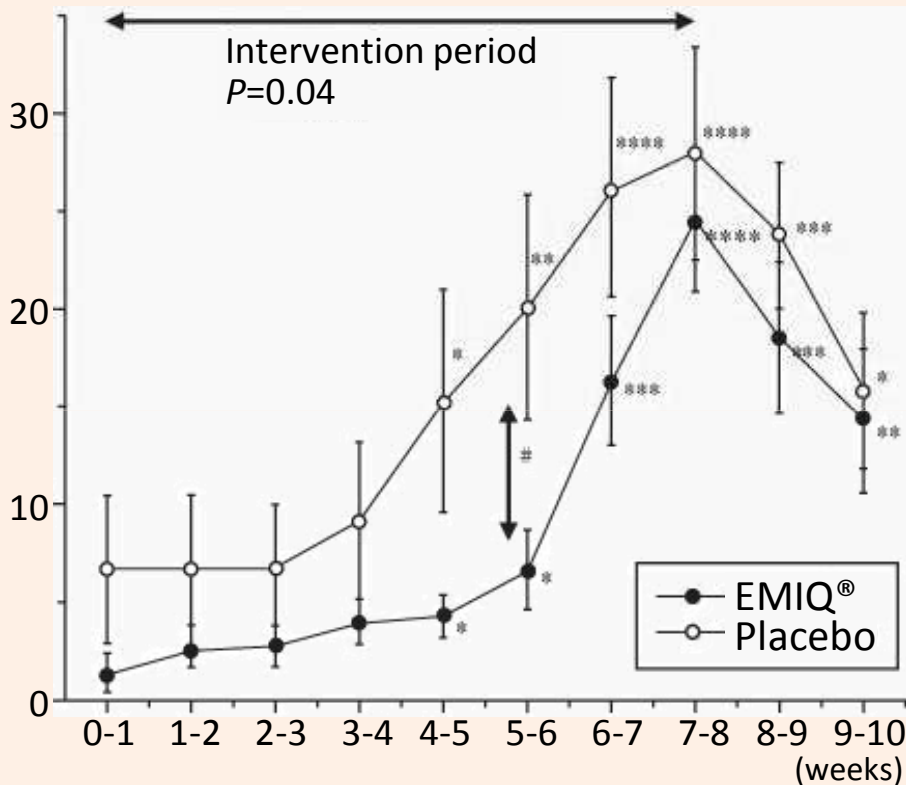
## *Double-blind study 2*

24 subjects took 100 mg EMIQ or a placebo for 8 weeks, starting 4 weeks prior to the onset of pollen release. During the entire study period, ocular symptom score for the EMIQ group was significantly lower. When limited to the pollen release period, ocular symptom scores and ocular congestion scores for the EMIQ group were also significantly lower. Nasal congestion did not differ in the two groups.

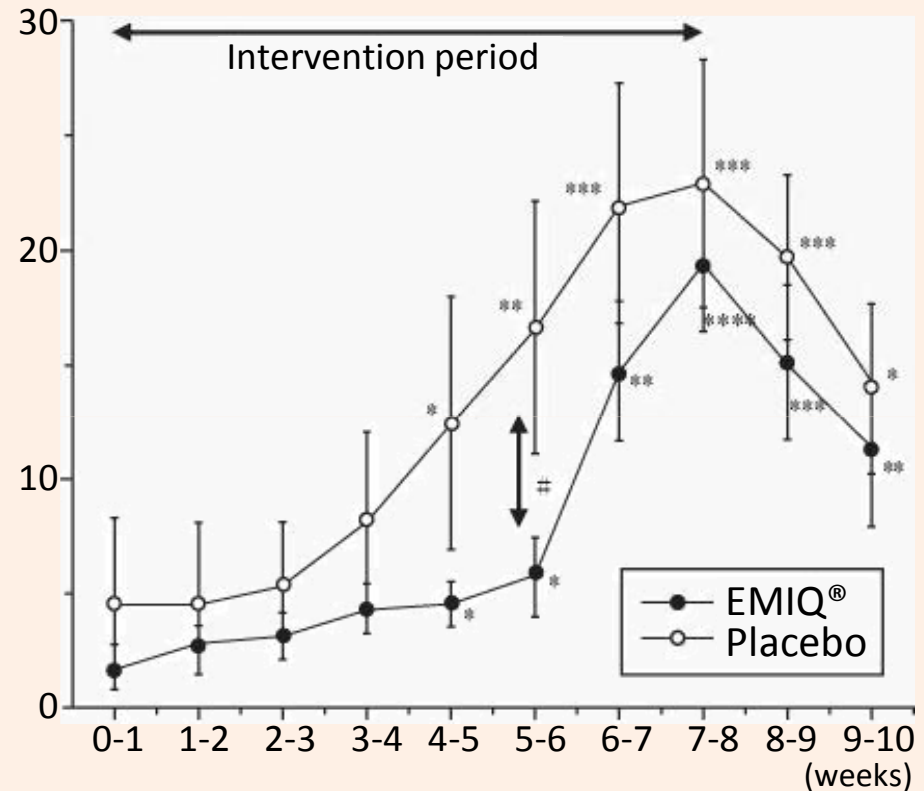
# EMIQ in Hayfever

## Double-blind study 2

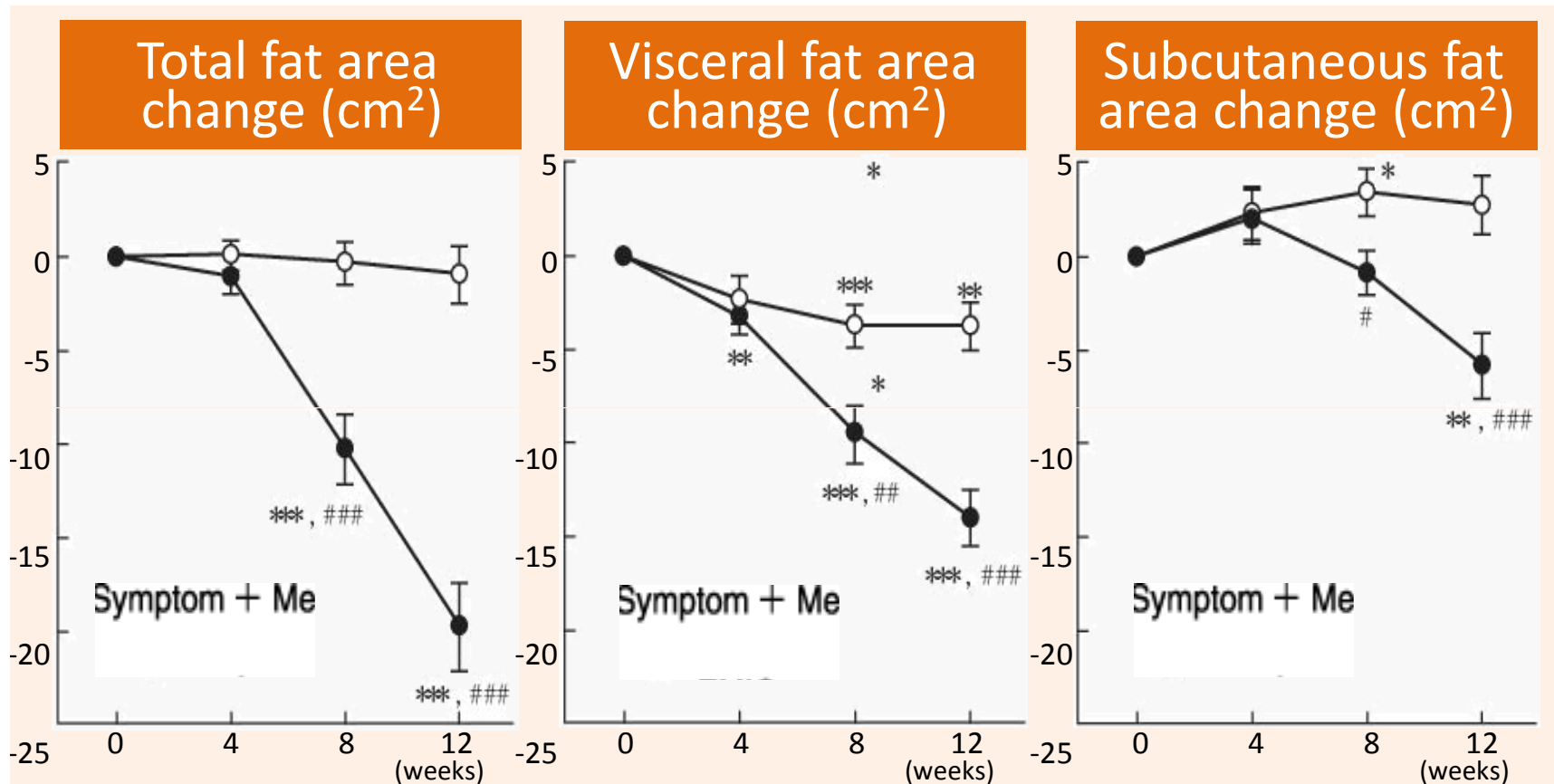
Ocular symptom + Medication score



Ocular symptom scores



# EMIQ (275 mg daily) Promotes Body Fat Reduction in Double-Blind Study



# ***What nutrients can enhance mitochondria?***

- All essential vitamins and minerals
- Cofactors in energy metabolism
  - Carnitine, Coenzyme Q10, Alpha Lipoic Acid, Ribose, etc.
  - Polyphenols, flavonoids, and other phytochemicals (PIGMENTS!!!!)
- Pyrroloquinoline quinone (PQQ)

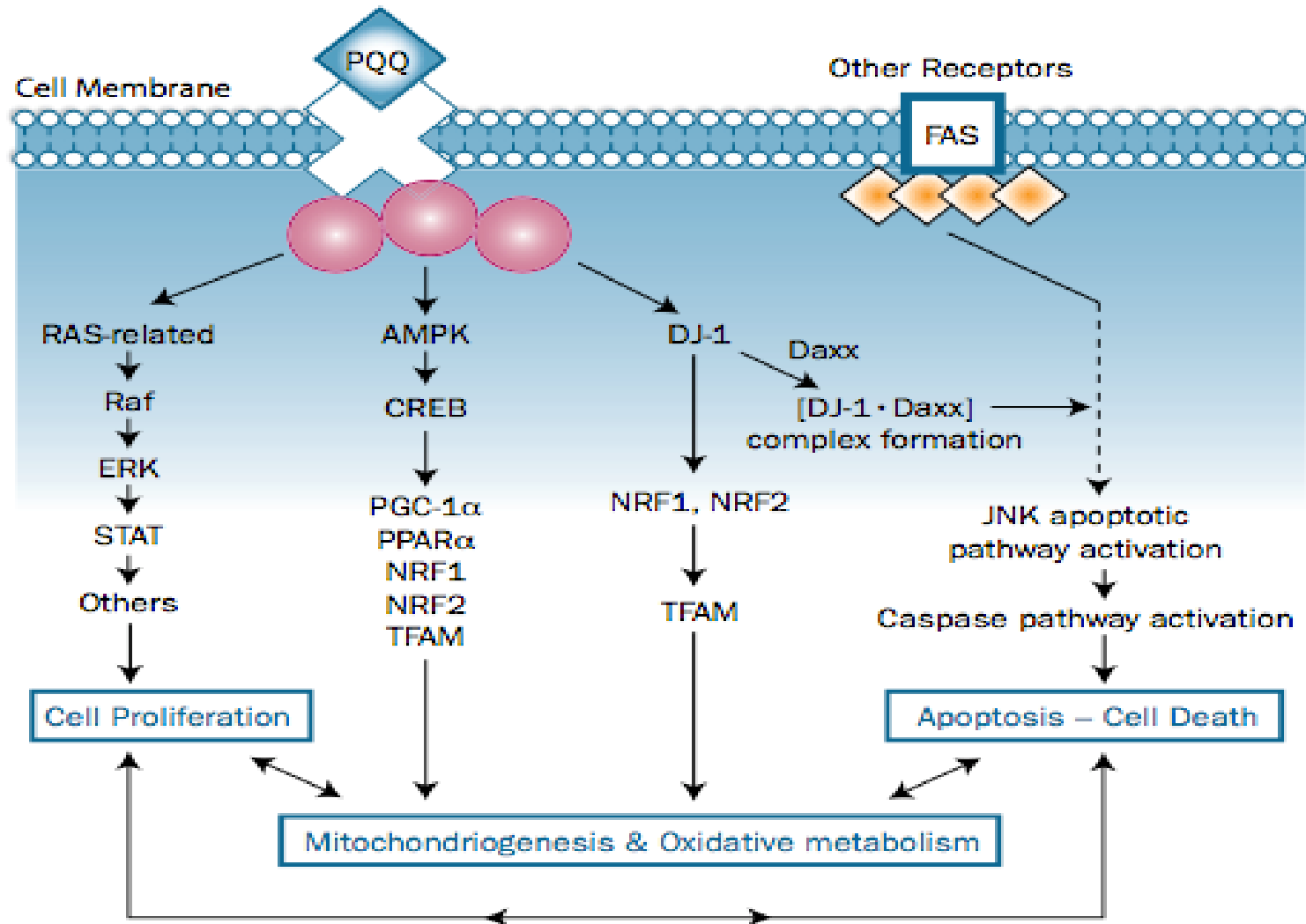
# ***Pyrroloquinoline Quinone (PQQ)***

- Vitamin-like cofactor
- Shown to be essential in mammalian nutrition in 1994
- Physiological functions:
  - Vital for mitochondrial function
  - Neuroprotective, promotes NGF
  - Memory restorative in animal and human studies
- Synergistic effect with CoQ10

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# PQQ and Cell Signalling



# ***PQQ: an Exceptional Antioxidant***

<b>Compound</b>	<b>Potential Number of Catalytic Cycles</b>
PQQ	20,000
Quercetin	800
Catechin	75
Epicatechin	700
Norepinephrine	200
Epinephrine	100
DOPA	20
6-OH-DOPA	20
Ascorbic Acid	4



# ***Pyrroloquinoline Quinone (PQQ)***

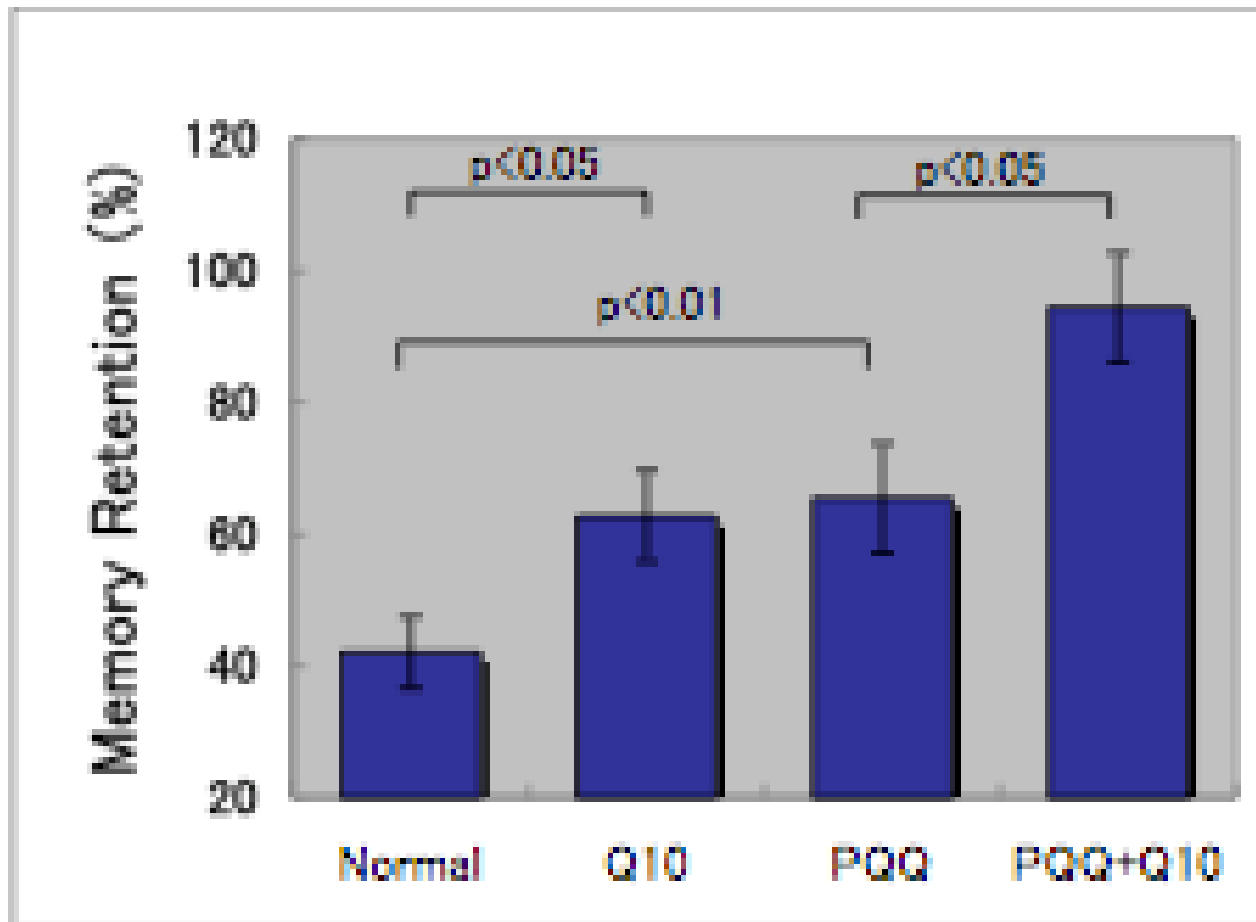
## **Results from Animal Studies**

- Reverses cognitive impairment caused by chronic oxidative stress and improve performance on memory tests in animal models.<sup>1,9</sup>
- *Supplementation stimulates the production and release of nerve growth factor.*<sup>1,10</sup>
- Protects against the self-oxidation of the DJ-1 gene, an early step in the onset of Parkinson's disease.<sup>1,11</sup>
- *Protects brain cells against oxidative damage in models of strokes.*<sup>1,12</sup>
- Blocks the formation of inducible nitric oxide synthase (iNOS), a major source of reactive nitrogen species (RNS) that are so damaging to brain cells.<sup>1,13</sup>
- *Protects the brain against neurotoxicity induced by other powerful toxins, including mercury, glutamate, and oxidopamine (a potent neurotoxin used by scientists to induce Parkinson's laboratory animals).*<sup>1,15,16</sup>
- Prevents development of alpha-synuclein, a protein associated with Parkinson's disease.<sup>1,17</sup>
- *Protects nerve cells from the damaging effects of the beta-amyloid-protein*

# Effects of PQQ & CoQ10 on Memory

## Animal Data

J Clin Biochem Nutr 2008;42:29-34.

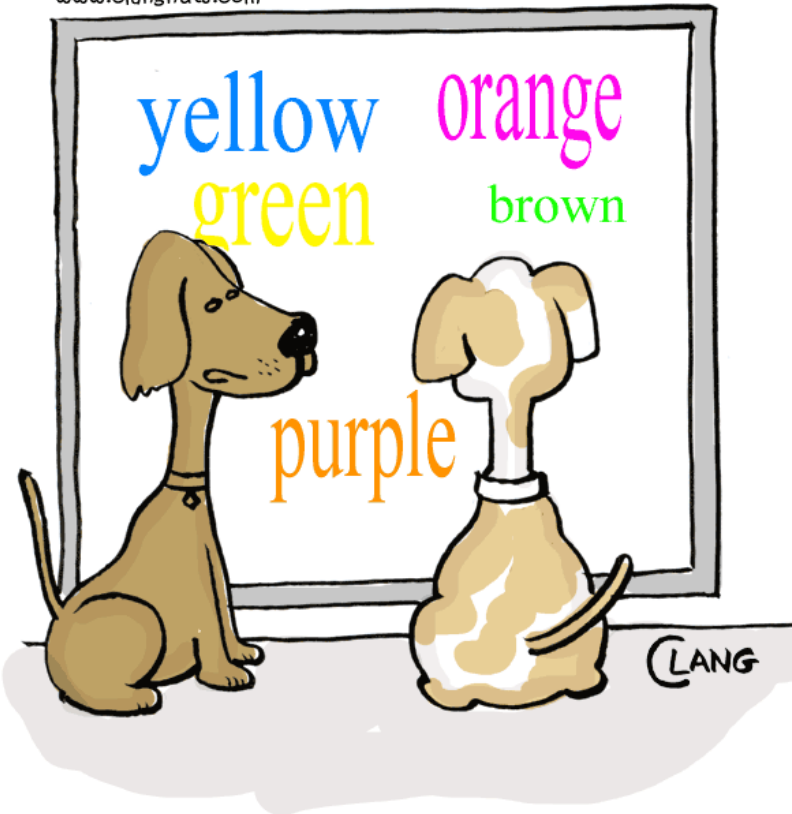


# Effects of PQQ & CoQ10 on

## Memory *Human Clinical Data*

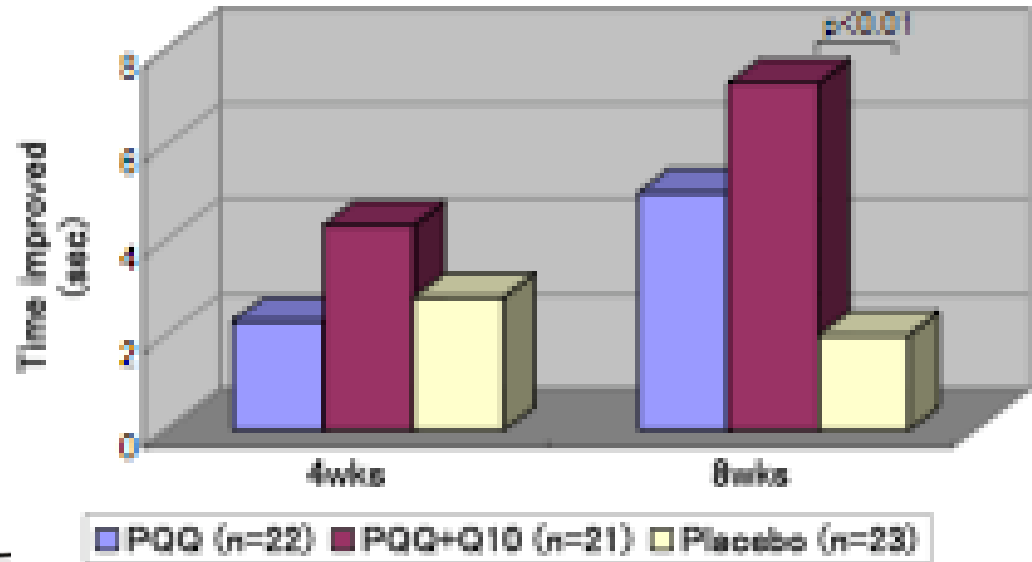
Effect of pyrroloquinoline quinone (PQQ) on mental status of middle-aged and elderly persons. FOOD Style. 2009;21:13(7):50-3.

www.clangnuts.com



...for some reason humans find these stroop tests really tricky!

### Stroop test



**PQQ = 20 mg/day**  
**PQQ + CoQ10 = 20 mg and 300 mg/day**  
**CoQ10 = 300 mg/day**

# **Dietary pyrroloquinoline quinone (PQQ) alters indicators of inflammation and mitochondrial-related metabolism in human subjects.** *Journal Nutritional Biochemistry* 2013;24:2076 - 2084

## Study Design:

Crossover study design, 10 subjects (5 females, 5 males) ages 21-34 years, ingested PQQ as a single on two separate occasions (0.2 mg/kg and 0.3 mg/kg).

## Outcomes measured:

Study 1, plasma and urine PQQ levels and changes in antioxidant potential.  
Study 2, indices of inflammation [plasma C-reactive protein, interleukin (IL)-6 levels]; and urinary metabolites related to energy metabolism.

## Results:

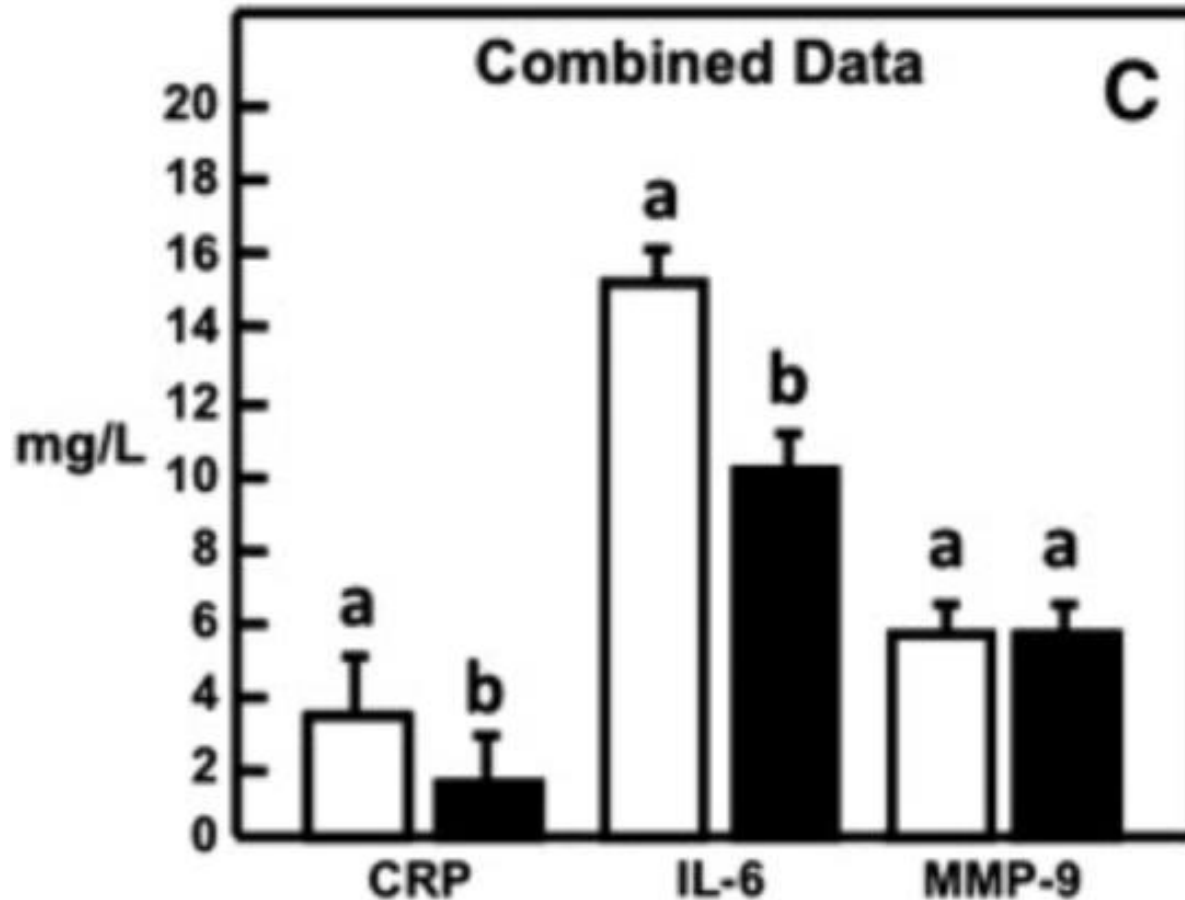
Study 1, increases in antioxidant potential were noted.  
Study 2, significant decreases in the levels of plasma C-reactive protein, IL-6 and urinary metabolites consistent with enhanced mitochondria-related functions.

## Significance:

Results are among the first to link systemic effects of PQQ in animals to corresponding effects in humans.

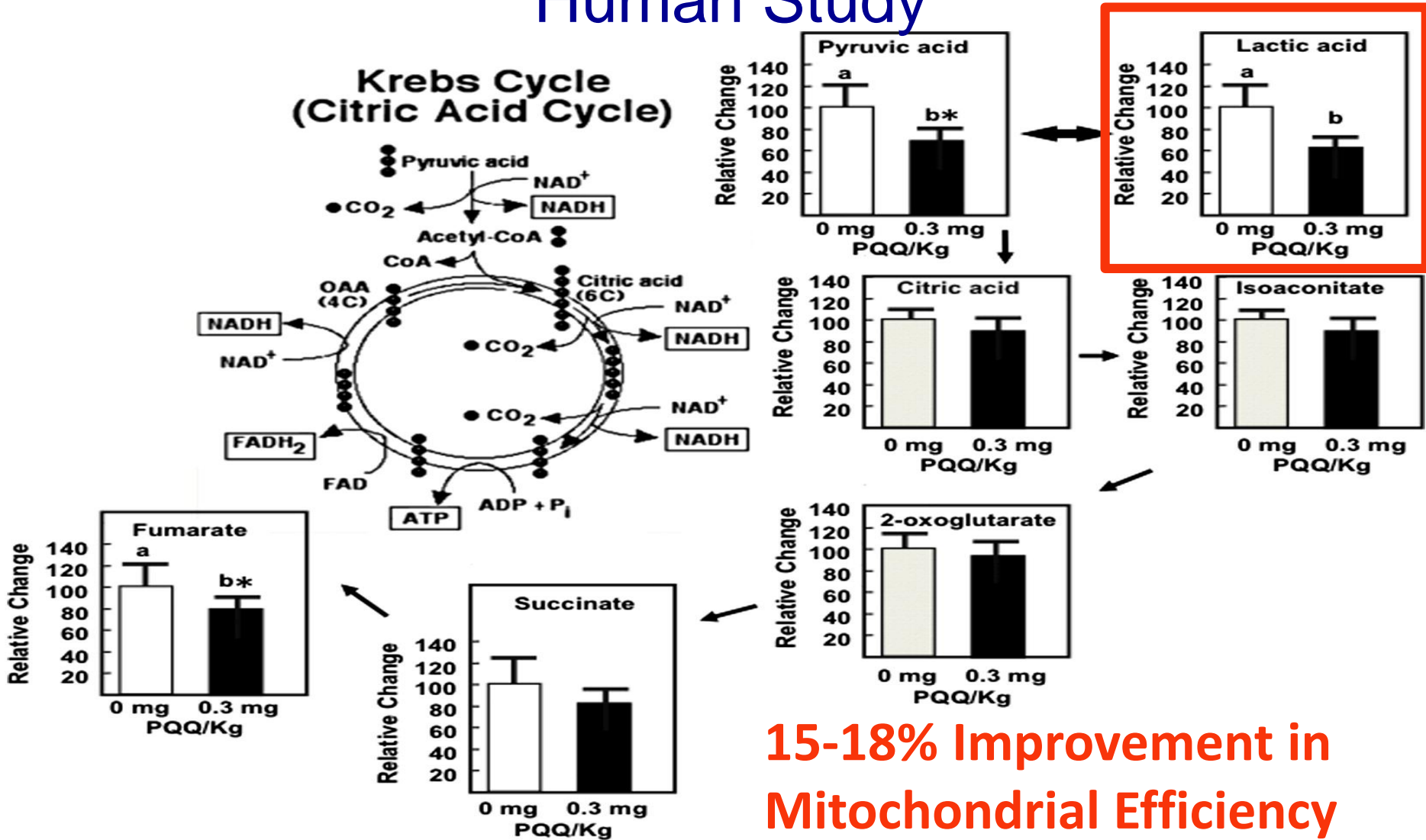
# *Effect of PQQ on CRP and IL-6*

## Human Study



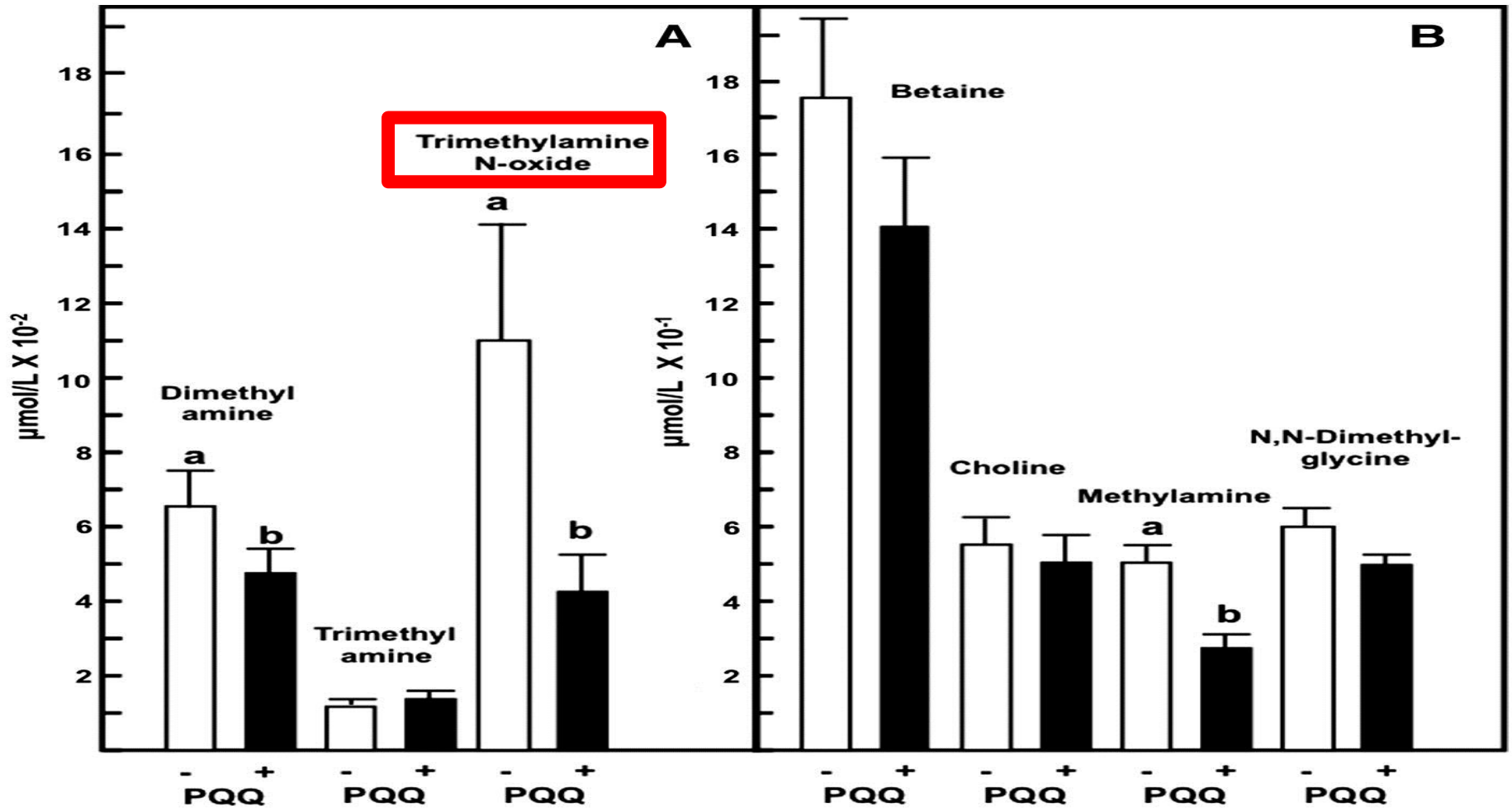
# Effect of PQQ on Energy Production

## Human Study



# Effect of PQQ on Energy Production

## Human Study



# ***Pyrroloquinoline Quinone (PQQ)***

## **Summary**

- Vital for mitochondrial function
- Promotes mitochondrial genesis
- Neuroprotective, promotes NGF
- Memory restorative in animal and human studies
- Reduces markers of oxidative damage and inflammation
- Synergistic effect with CoQ10
- Dosage recommendation: 10 to 20 mg daily