

Coenzyme Q (ubiquinone)

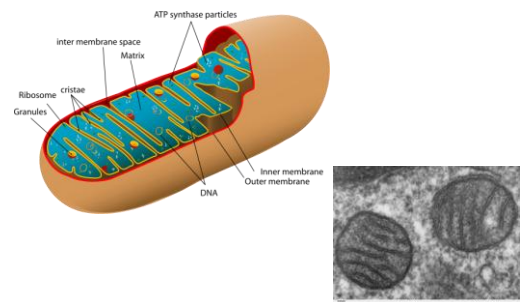
- Can be a challenge to determine if a particular supplement is beneficial or harmful, in part because of complex biochemical interactions
- We'll look at Co-enzyme Q10 as an example.

Background

- Coenzyme Q (ubiquinone) is sold as an anti-oxidant.
- Many people take Q as a life-extension supplement.
- Also used to treat certain cardiac conditions

- Coenzyme Q is a carrier of electrons in the mitochondrial Electron Transport Chain.
- Electron transport create a proton gradient across the inner membrane.
- Mitochondria use this proton gradient in synthesis of ATP.
- Electrons that escape from the electron transport chain generate free radicals

Electron transport occurs in the inner mitochondrial membrane in eukaryotes.



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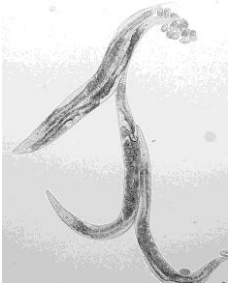
Q functions:

- *Anti-oxidant*
 - accepts electrons and helps move them along the Electron Transport Chain
- *Pro-oxidant*
 - generates superoxide, a reactive oxygen species

Q6, Q7, Q8, Q9, and Q10

- Coenzyme Q can have a variable length side chain, with typically 6 to 10 subunits, hence Q6, Q7, Q8, Q9, and Q10.
- Different species tend to produce Q with a particular length side chain
 - Q10 in human
 - Q9 in worm
 - Q8 in bacteria

Q mutants in *C. elegans* worms



commons.wikimedia.org/wiki/File:C_elegans_DIC_3.jpg by Polyhedron

Q mutants in *C. elegans* worms

- Clk-1 mutants in worms lack endogenous Q9
- The missing clk-1 gene encodes an enzyme responsible for final step in Q synthesis
- Clk-1 mutants live twice as long as wildtype worms.
- What happens if we suppress Q synthesis in normal (wild type) worms?

Silencing of Ubiquinone Biosynthesis Genes Extends Lifespan of Worms

Asencio, Rodrigues-aguilera et al

- Examine the effect of RNA interference (RNAi) directed at putative Q9 synthesis genes in worms
 - during Q9 biosynthesis and Q8 intake
 - Putative Q9 genes were identified by homology to Q6 biosynthesis genes in yeast
- Examine the lifespan and mitochondrial respiratory chain activity of worms treated with RNAi

Results

- Using RNA interference, 8 genes were identified that participate in Q9 biosynthesis in worms.
- RNA interference of Q9 biosynthesis genes extends lifespan.
- Worms treated with RNAi produce less superoxide anions (30-50% less).

Results

- At least 8 genes participate in Q9 biosynthesis.
- Silencing the genes results in:
 - lowered Q9 levels
 - lower superoxide production (in ETC)
 - extended lifespan
 - less damage to macromolecules in mitochondria.
- Findings support the endogenous oxidative stress hypothesis.

- Superoxide produced by Q10 is eventually de-activated by alpha lipoic acid.
- Taking Q10 as a supplement without increasing lipoic acid will likely increase damaging superoxide levels