Mitochondria & Ageing
Its critical role in health, longevity, illness, and death

Extracted from the presentation by Lee Know, ND, www.KnowGuff.com on May 12, 2015
* See Footnotes

OVERVIEW
1. Mitochondrial function lies at the root of many age-related degenerative diseases
2. Protecting mitochondrial function best done by coordinated approach of exercise, lifestyle, and nutrition
3. A comprehensive nutritional approach includes CoQ10, magnesium, L-carnitine, and PQQ

What is it?
Tiny organelle (functional part of a cell) that produce energy

Free-Radicals
- Highly-reactive unstable molecules
- Can inflict damage to DNA*, proteins, membranes, etc.
- Mitochondria* are the primary site of free-radical production
- damage mitochondrial DNA, which causes mitochondrial dysfunction

Mitochondrial Dysfunction
Step-by-step, things start to fall apart…
1. Cellular energy deficit
2. Dysfunctional processes that require ATP*
3. Cellular dysfunction
4. Organ/tissue dysfunction
5. Degenerative diseases & ageing, which leads to mitochondria death and tissue atrophy (wasting away)

Mitochondrial Disease
Primary disease (inherited)
- Doesn't always follow Mendel's Laws*
- Autosomal recessive/dominant OR maternal inheritance
- Mismatched nDNA to mtDNA
- Incredibly variable clinical presentations!!!

Secondary disease (acquired)
- Type 2 diabetes
- Alzheimer's, cardiovascular disease
- Exercise intolerance, fatigue, sarcopenia
- Many common age-related disease show mitochondrial dysfunction at the root

Restore, Repair, Reclaim
1. Clean, nutrient-dense diet
2. Avoid environmental toxins
3. Calorie-restriction: fewer electrons entering ETC., proven to extend lifespan & health span
4. Exercise: Essential and mandatory in any protocol for mitochondrial health, Induce mitochondrial biogenesis, Exercise Paradox
5. Nutrition,& Supplementation: Improve mitochondrial function & bioenergetics

Nutrition,& Supplementation

PQQ
Intake from foods: 0.01 –0.4 mg/day
Therapeutic dose for cognition: 20 mg/day •

Coenzyme Q10
Role in mitochondrial function:
Component of ETC
• Membrane stabilizer
• Regulates gene expression
• Cofactor in UCPs & mPTP, etc.

Magnesium
70-80% are deficient
• Role in bioenergetics: involved in ATP production (enzymes of glycolysis & TCA cycle), cofactor for ATPase, stabilizes ATP (Mg-ATP)
• Required for muscle relaxation: vasoconstriction leads to poor delivery of nutrients/fuel and O2

L-Carnitine
60-70% of ATP from fatty acids
Nearly 100% of dietary FAs are long-chain
Role in bioenergetics: L-Carnitine transports long-chain FA into mitochondria, modulates intracellular CoA homeostasis, removes excess acyl groups
Acetyl-L-Carnitine crosses blood-brain barrier

Conclusion
Mitochondrial function lies at the root of many age-related degenerative diseases
Protecting mitochondrial function best done by coordinated approach of exercise, lifestyle, and nutrition
Supplements: PQQ, CoQ10, Magnesium, Acetyl-L-Carnitine: foundational to a comprehensive nutritional approach.

* See Footnotes

FOOTNOTES/Glossary

Adenosine triphosphate (ATP)
Adenosine triphosphate (ATP) is a nucleoside triphosphate used in cells as a coenzyme, often called the "molecular unit of currency" of intracellular energy transfer.[1]

ATP transports chemical energy within cells for metabolism. It is one of the end products of photophosphorylation, cellular respiration, and fermentation and used by enzymes and structural proteins in many cellular processes, including biosynthetic reactions, motility, and cell division.[2] One molecule of ATP contains three phosphate groups, and it is produced by a wide variety of enzymes, including ATP synthase, from adenosine diphosphate (ADP) or adenosine monophosphate (AMP) and various phosphate group donors. Substrate-level phosphorylation, oxidative phosphorylation in cellular respiration, and photophosphorylation in photosynthesis are three major mechanisms of ATP biosynthesis.

Metabolic processes that use ATP as an energy source convert it back into its precursors. ATP is therefore continuously recycled in organisms: the human body, which on average contains only 250 grams (8.8 oz) of ATP,[3] turns over its own body weight equivalent in ATP each day.[4]

Deoxyribonucleic acid(DNA)
Deoxyribonucleic acid(DNA) is a molecule that encodes the genetic instructions used in the development and functioning of all known living organisms and many viruses. DNA is a nucleic acid; alongside proteins and

carbohydrates, nucleic acids compose the three major macromolecules essential for all known forms of life. Most DNA molecules consist of two biopolymer strands coiled around each other to form a double helix. The two DNA strands are known as polynucleotides since they are composed of simpler units called nucleotides. Each nucleotide is composed of a nitrogen-containing nucleobase—either guanine (G), adenine (A), thymine (T), or cytosine (C)—as well as a monosaccharide sugar called deoxyribose and a phosphate group. The nucleotides are joined to one another in a chain by covalent bonds between the sugar of one nucleotide and the phosphate of the next, resulting in an alternating sugar-phosphate backbone. According to base pairing rules (A with T and C with G), hydrogen bonds bind the nitrogenous bases of the two separate polynucleotide strands to make double-stranded DNA.

DNA is well-suited for biological information storage. The DNA backbone is resistant to cleavage, and both strands of the double-stranded structure store the same biological information. Biological information is replicated as the two strands are separated. A significant portion of DNA (more than 98% for humans) is non-coding, meaning that these sections do not serve as patterns for protein sequences.

Mendel's law

Any of the principles first proposed by Gregor Mendel to describe the inheritance of traits passed from one generation to the next. There are three:
1. Law of segregation) states that during the formation of reproductive cells (gametes), pairs of hereditary factors (genes) for a specific trait separate so that offspring receive one factor from each parent.

2. Law of independent assortment) states that chance determines which factor for a particular trait is inherited.
3. Law of dominance) states that one of the factors for a pair of inherited traits will be dominant and the other recessive, unless both factors are recessive.

Organelles: A differentiated structure within a cell, such as a mitochondrion, vacuole, or chloroplast, that performs a specific function.

Mitochondria

Mitochondria are often referred to as the powerhouses of the cells. They generate the energy that our cells need to do their jobs. For example, brain cells need a lot of energy to be able to communicate with each other and also to communicate with parts of the body that may be far away, to do this substances need to be transported along the cells, which needs lots of energy. Muscle fibres also need a lot of energy to help us to move, maintain our posture and lift objects.

Mitochondria generate chemical energy, similar to the type of energy you get from a battery. The energy made by the mitochondria is in the form of a chemical called adenosine triphosphate or ATP for short. ATP is an energy currency that every cell in our body can use and it keeps us alive. The machinery that the mitochondria use to make ATP is called the electron transport chain. This chain is made up of 4 complexes which are groups of proteins that work together to carry out their function, the 5th complex is responsible for the final step of the energy generation. It is found in the inner mitochondrial membrane and parts of the first, third, fourth and fifth complexes are coded for by the mitochondrial DNA. In order for energy to be generated several steps have to occur.

Electrons are particles within an atom that are negatively charged, along with the other particles (protons and neutrons) they make up everything in the universe and they are very important in biology. Electrons are passed between the complexes of the electron transport chain and enable the cells to generate energy. The first complex accepts the electrons that are produced from the degradation of the food we eat. As it passes the electrons to the third complex in the chain protons (positively charged hydrogen atoms) are moved across the inner mitochondrial membrane. At complex three the electrons from complex one are joined by others donated by complex two. Complex three passes these electrons onto complex four and in the process moves more protons across the inner mitochondrial membrane. Within complex four the electrons are joined to oxygen to produce water, alongside one

final movement of protons. Since so many protons have now been moved across the membrane the amount of them is higher on one side of the membrane than the other, this creates a gradient. Complex five then uses this gradient to produce ATP. The proton gradient rotates this final complex and with each rotation an ATP is made. For every cycle of the electron transport chain over 30 ATPs are produced, this shows how efficient energy generation is within the mitochondria.

They help maintain the environment within our cells.

The environment within our cells is closely monitored and maintained at the optimum conditions. Mitochondria are crucial to help preserve this environment and their most valuable contribution to this process is that they take up calcium. Calcium is important within cells as a signalling molecule, but this we mean that similar to flares or a 999 call calcium alerts the cell that something needs to happen, a process needs to begin and the cell needs to respond to what is happening. This signalling needs to be regulated and so the mitochondria store calcium and release it when it is required. Too much free calcium within the cell would be detrimental to the finely tuned regulation of processes within the cell.