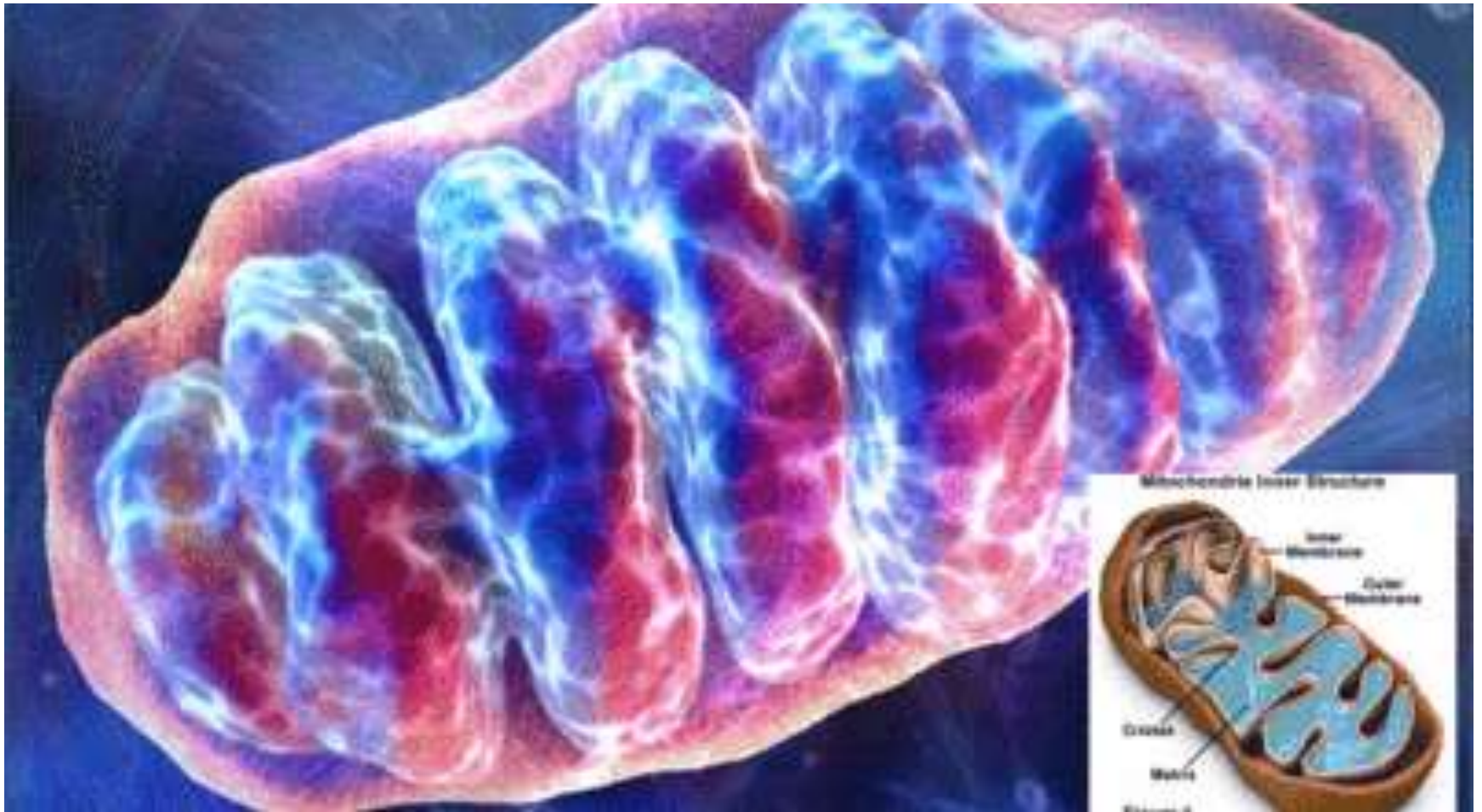
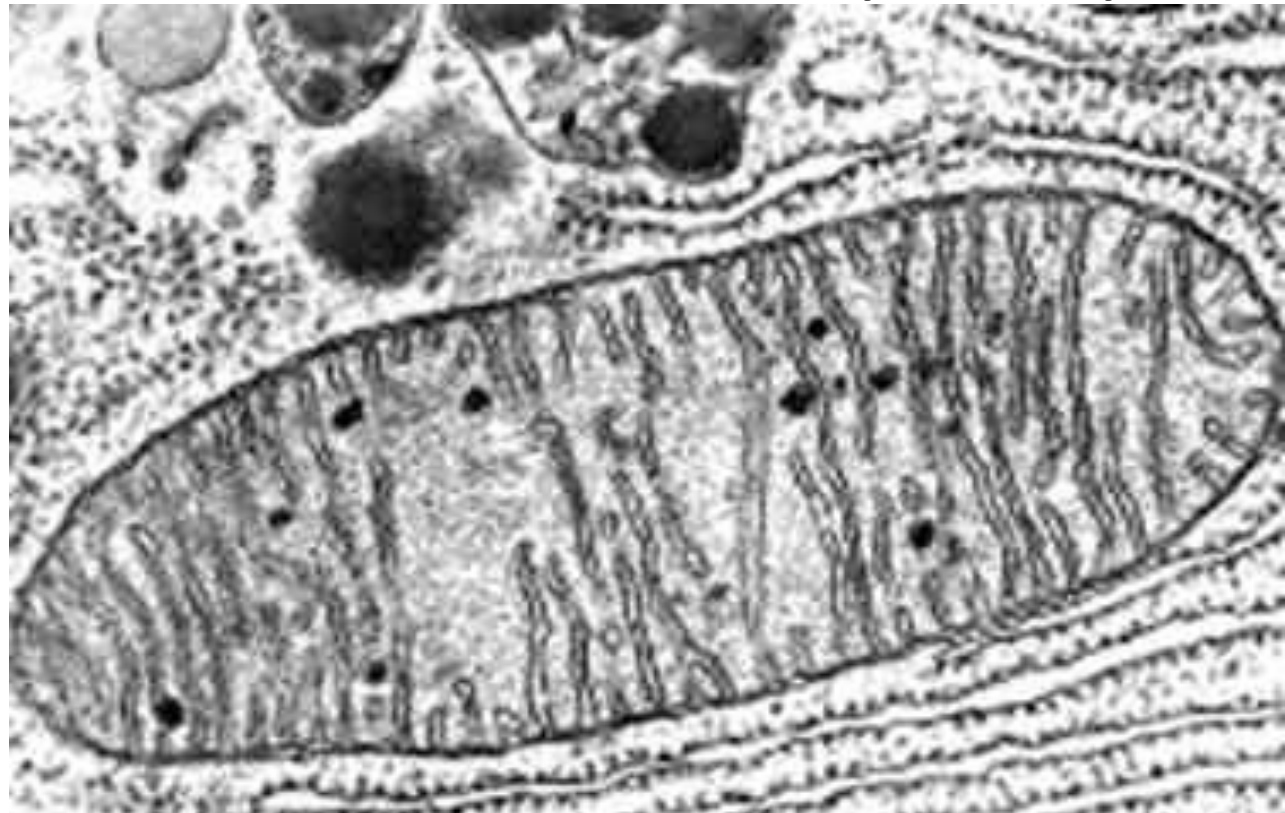


Mitochondria, Metals and Dementias



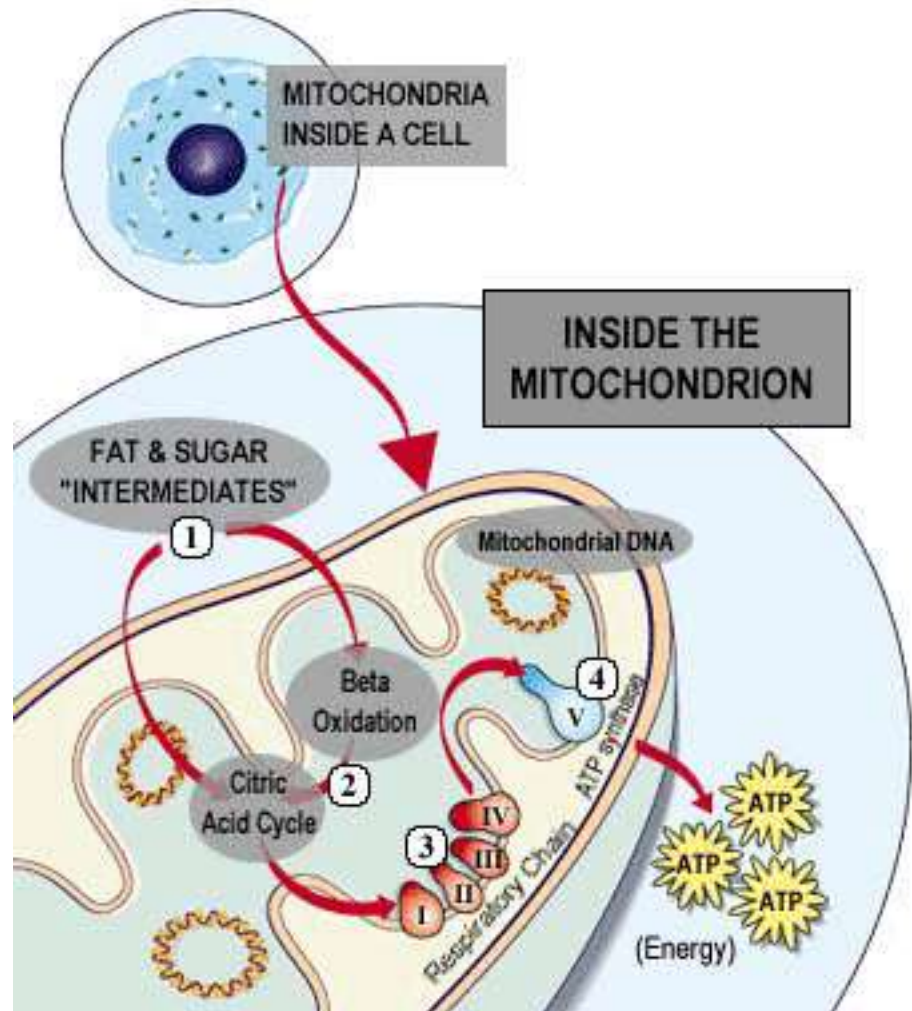
Glucose / H₂O / O₂

- 7-7-7 rule (7 weeks food/ 7 days water/ 7 minutes oxygen)
- System will work better (but only briefly) w/o oxygen



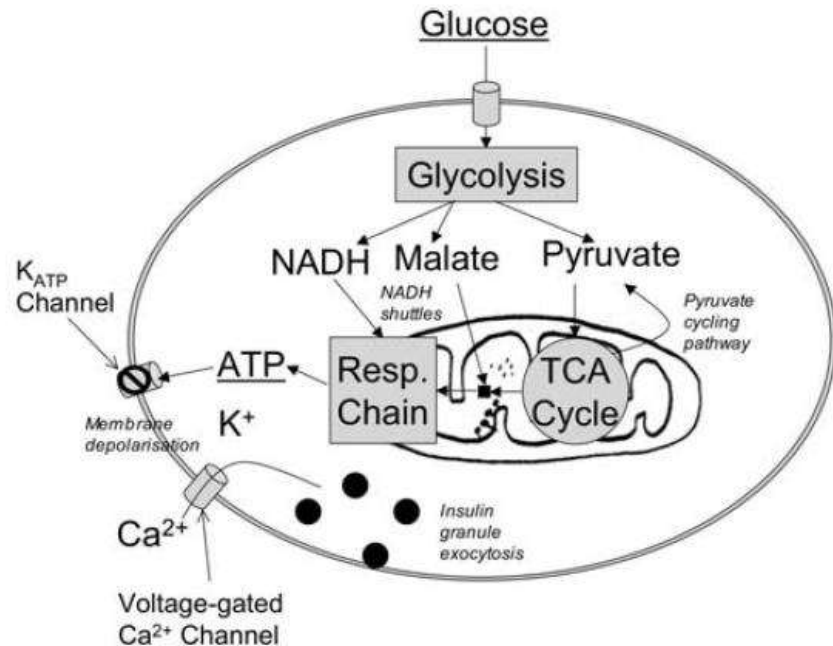
Mitochondria primer

- <http://www.youtube.com/watch?v=TgJt4KgKQJI&feature=related>



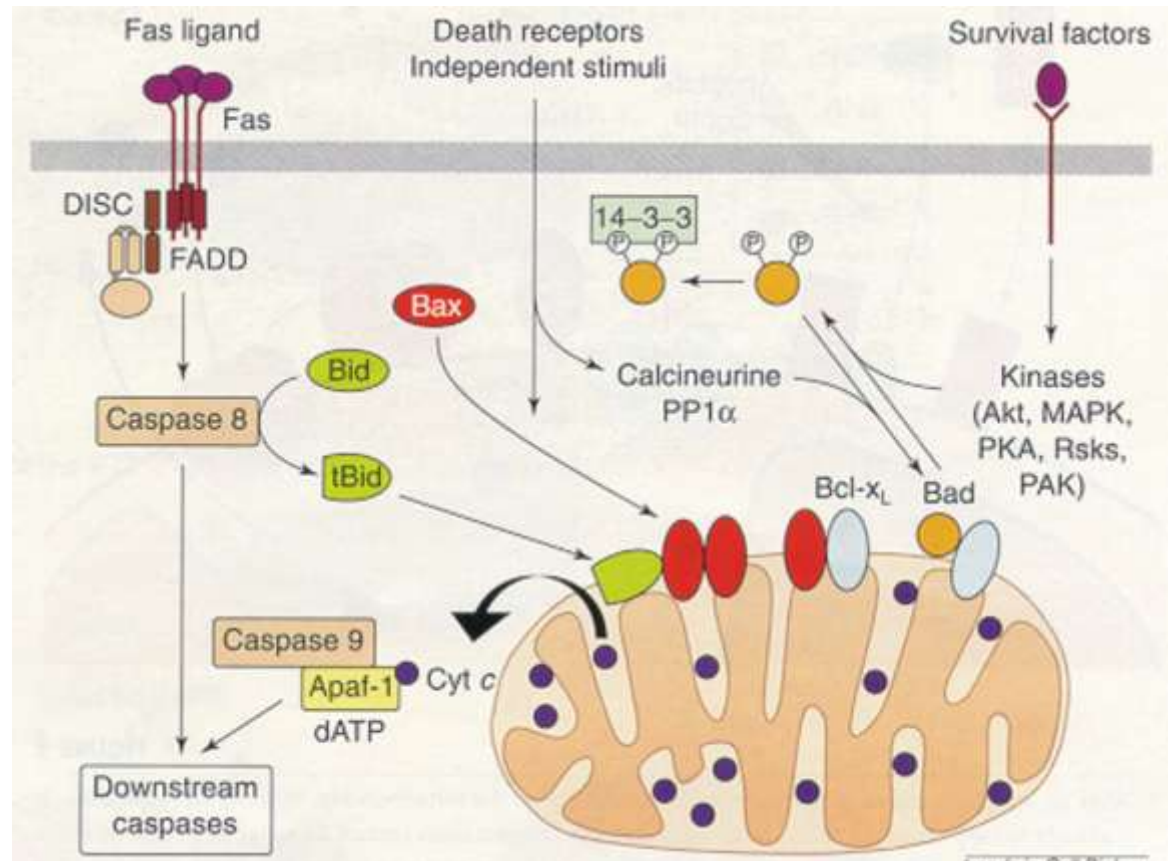
Mitochondria

- Highly basic environment
- Have own DNA
- Process Glu (pyruvate) and O₂



Mtc genes

- <http://www.youtube.com/watch?v=yF7esxWJj1Q>



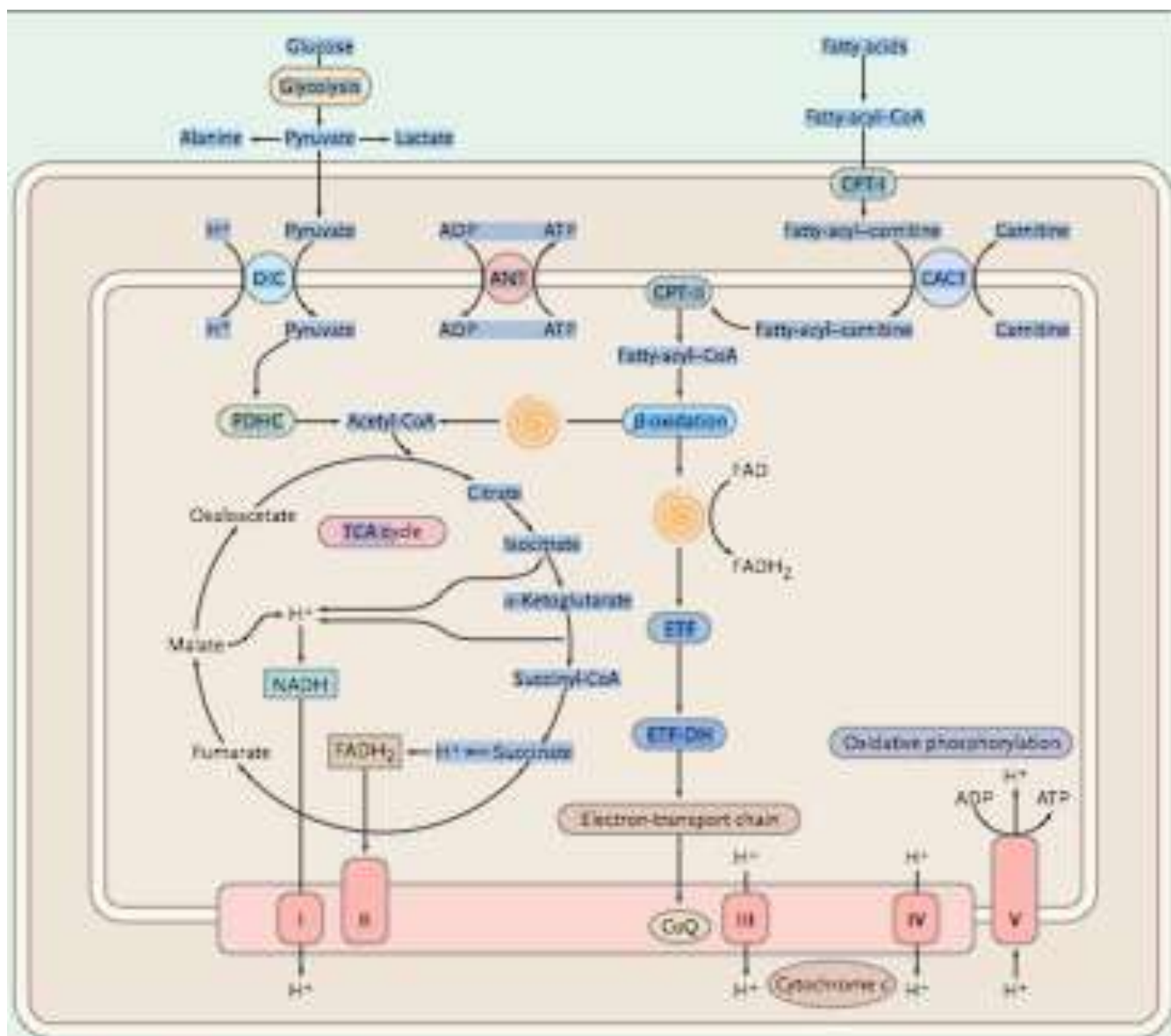


Figure 1. Selected Metabolic Pathways in Mitochondria.

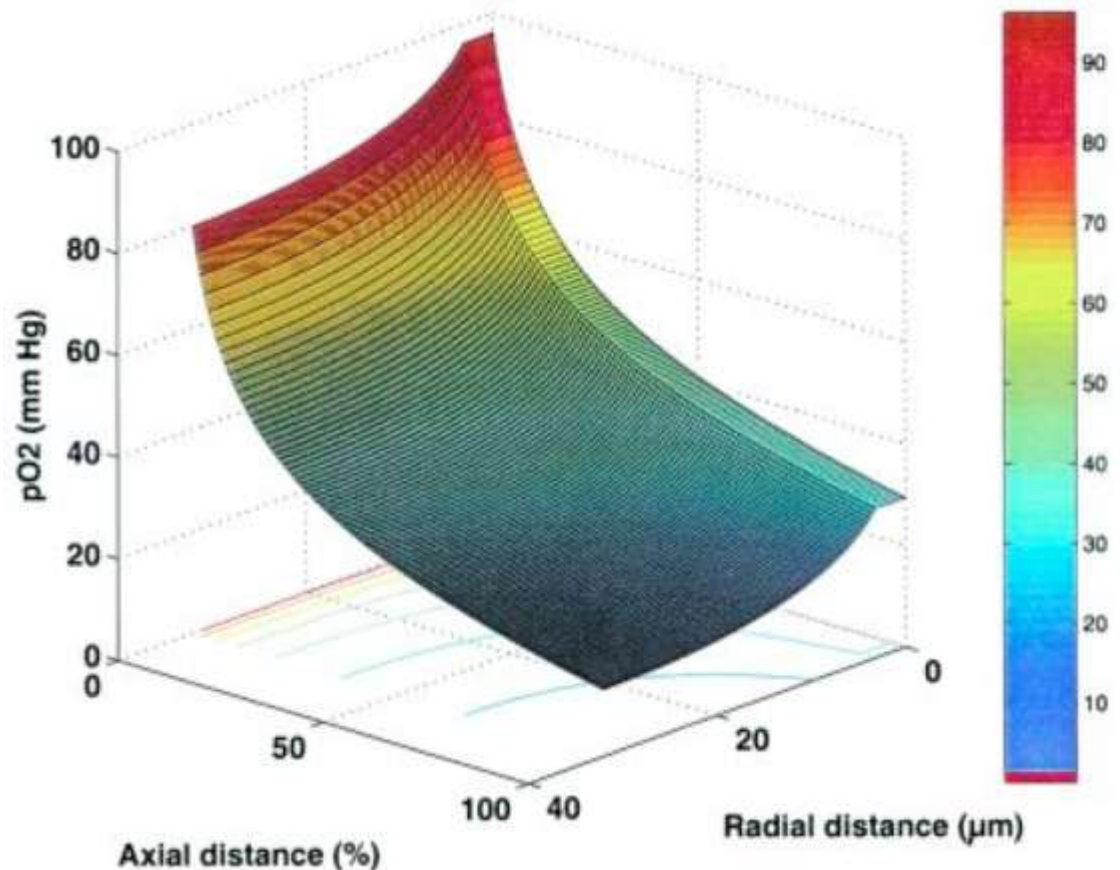
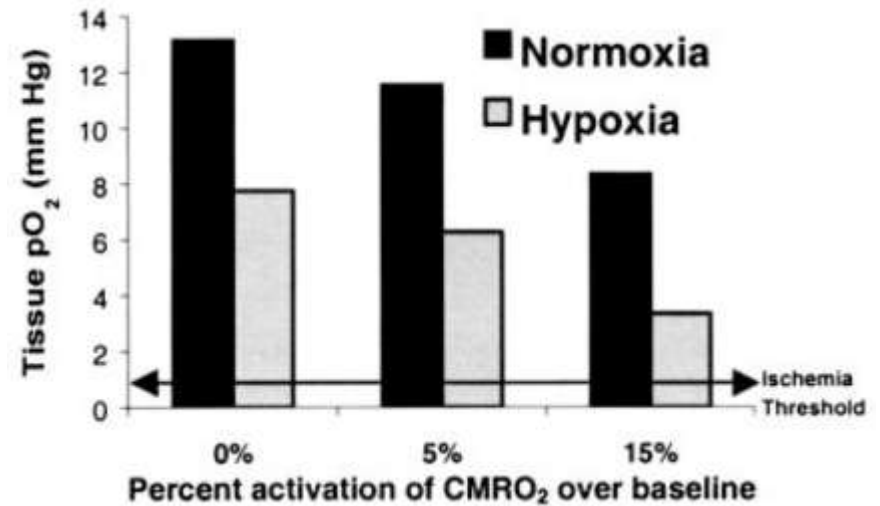
The spirals represent the spiral of reactions of the β -oxidation pathway, resulting in the liberation of acetyl-coenzyme A (CoA) and the reduction of flavoprotein. ADP denotes adenosine diphosphate, ATP adenosine triphosphate, ANT adenine nucleotide translocator, CACT carnitine-acyl-carnitine transferase, CoQ coenzyme Q, CPT carnitine palmitoyltransferase, DIC dicarboxylate carrier, ETF electron-transfer flavoprotein, ETF-DH electron-transfer dehydrogenase, FAD flavin adenine dinucleotide, FADH₂ reduced FAD, NADH reduced nicotinamide adenine dinucleotide, PDHC pyruvate dehydrogenase complex, TCA tricarboxylic acid, I complex I, II complex II, III complex III, IV complex IV, and V complex V.

Apoptosis

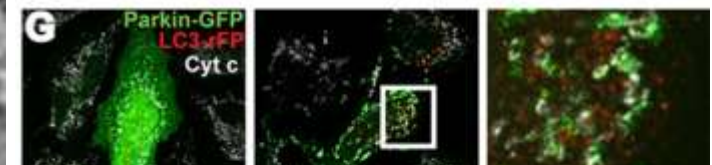
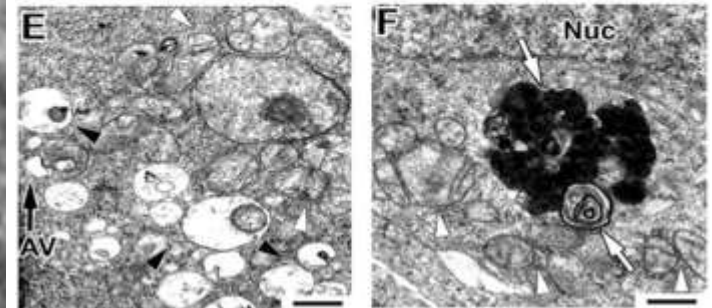
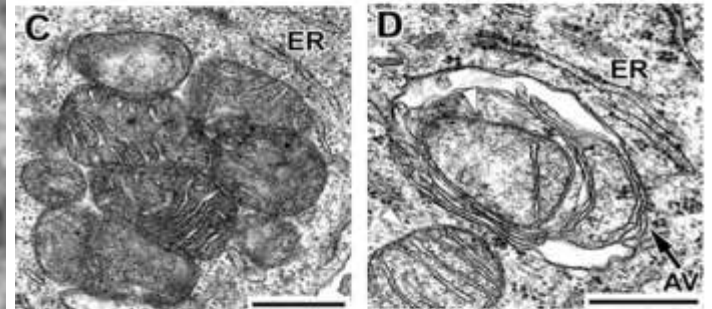
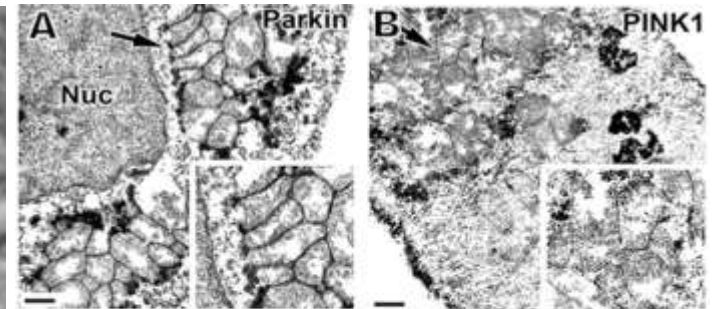
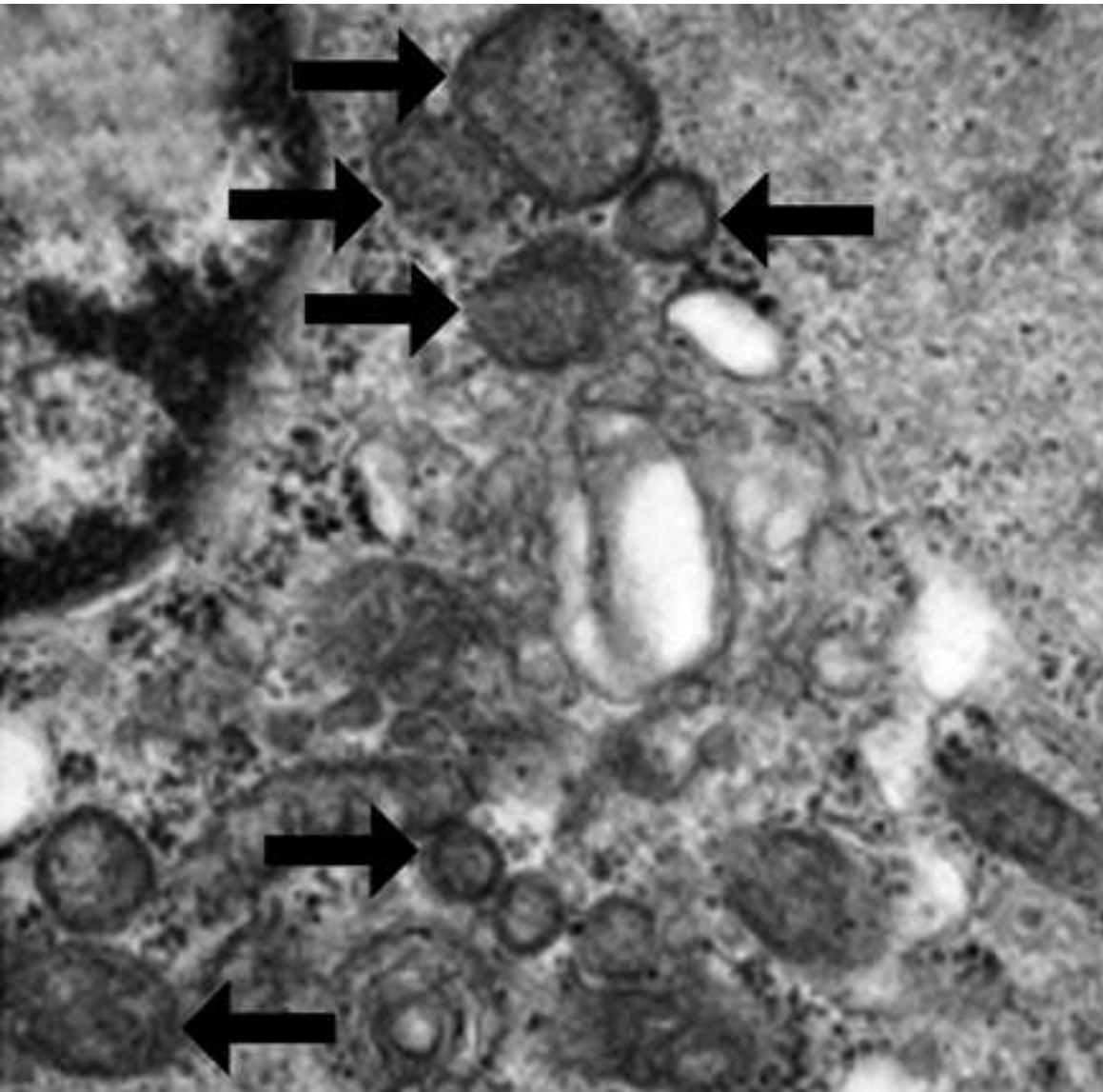
- <http://www.youtube.com/watch?v=xkASer3gEnc&NR=1> (1.33 in vitro)
- <http://www.youtube.com/watch?v=i0SuQrJUi-4&feature=related> (1.31 in vivo)
- <http://www.youtube.com/watch?v=nk3dZyUZJCc&feature=related> (5m/cartoon)
- <http://www.youtube.com/watch?v=v1PWcX66ucl&feature=related> (1.46 Mtc)

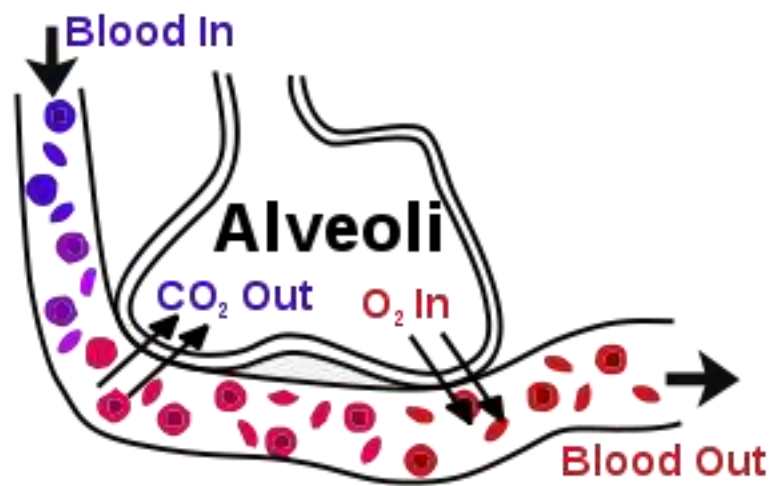
Oxygen gradients

- Radial entry into membranes
- Diffusion selective when PO is low
- Intracellular gradients as much as 1/70th of water
- Overall low gradient
- O₂ tensions lower in clusters than in basic functional areas
- O₂ gradients determine O₂ distributions in cell.
- Clusters need higher gradients and PO
- Higher O₂ intake = Mtc cluster O₂ availability



Mitochondria Clusters





Oxygen transport video

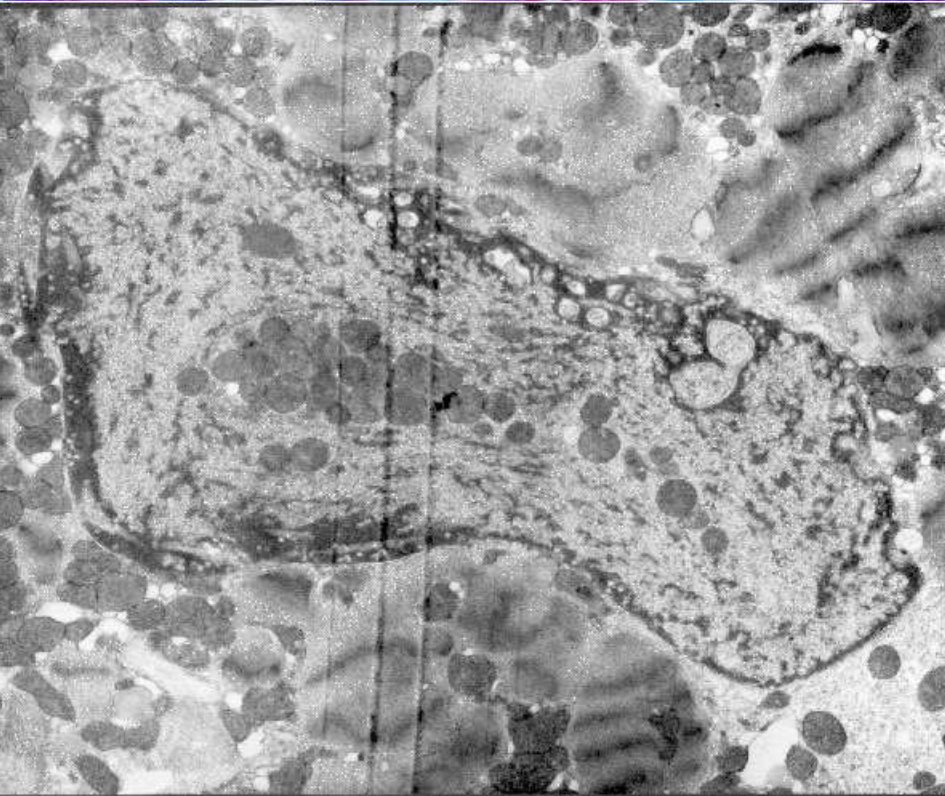
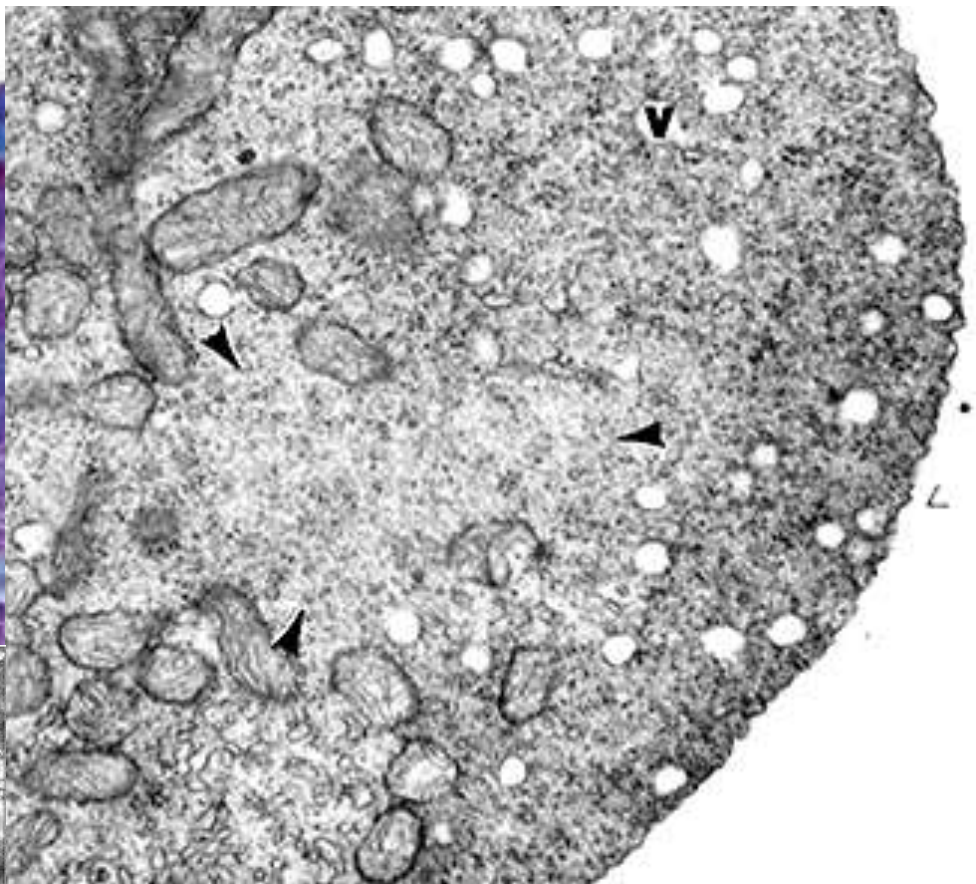
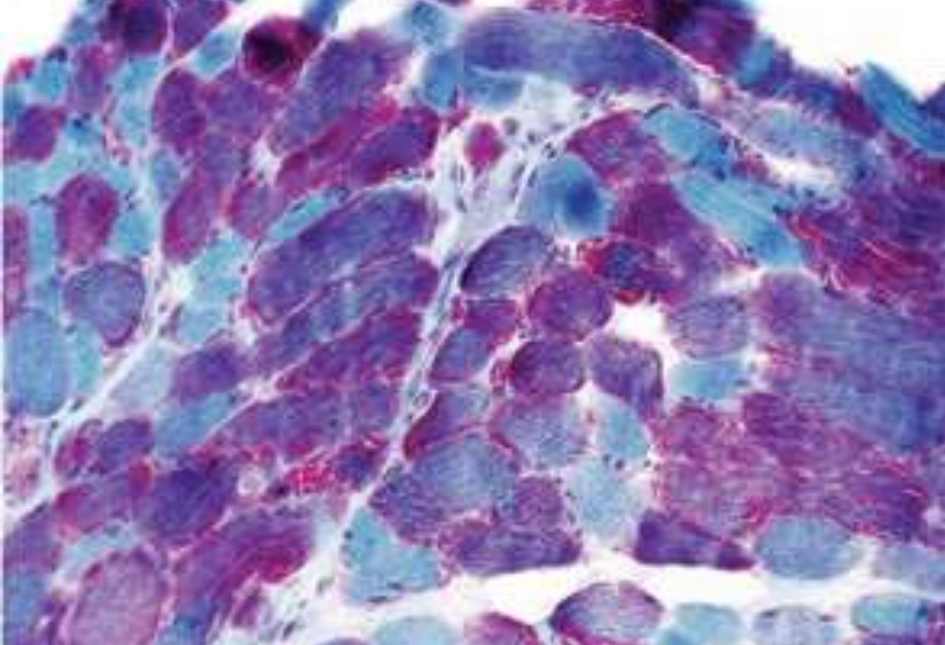
<http://www.youtube.com/watch?v=WXOBJEXxNEo&feature=related>

CO2 video

<http://www.youtube.com/watch?v=x26TWL3VKMg&NR=1>

Respiratory video to 4 minutes

<http://www.youtube.com/watch?v=GERsMFWYZrw&feature=related>



Mitochondria – Harvard Hughes 2m

<http://www.youtube.com/watch?v=RrS2uROUjK4>

Metals

Oxygen, ATP and the biochemical cascade leading to Alzheimer's

Metals and Elements involved

Cu

Zn

Fe

Ca

K

NO

Roles

- Cu for learning, memory and basic AP
- Ca for all neuronal functions after AP
- Zn for level of energization in neuron
- Fe for inhibition between Cu based firings
- Li
- Ka
- NO (begin at 1.20) NO Pt 2 (Ignarro)

Reactions

- [Na and Ka](#) (Ka releases H ions)
- [NO + Cu = dehydration?](#)
- [NO + O2 Symbiotic association](#)
- [Arginine = NO Animal sources](#)
- Sources: dairy products (e.g. [cottage cheese, ricotta, milk, yogurt, whey protein drinks](#)), beef, pork (e.g. [bacon, ham](#)), [gelatin](#), poultry (e.g. [chicken and turkey light meat](#)), wild game (e.g. [pheasant, quail](#)), seafood (e.g. [halibut, lobster, salmon, shrimp, snails, tuna](#))
- Plant sources
- [wheat germ and flour, buckwheat, granola, oatmeal, peanuts, nuts \(coconut, pecans, cashews, walnuts, almonds, Brazil nuts, hazelnuts, pinenuts\), seeds \(pumpkin, sesame, sunflower\), chick peas, cooked soybeans, *Phalaris canariensis* \(canaryseed or ALPISTE\)](#)

Cytochrome C

- [Cytochrome C](#) found in Complex II and IV
- Oxygen dependent
- Water soluble, highly plastic, varying pH
- 104 amino acid polypeptide chain
- Hydrophobic side chains surround heme
- Isoelectric point (number of + and – charges near pH 10)
- Highly basic inner Mtc matrix

Fe³/Fe²

Fe²⁺ is redox state – allows Cyt C to cross to inner membrane

Fe³⁺ non-redox – escapes to contribute to AD

[http://www.cell.com/abstract/S0092-8674\(10\)00938-4](http://www.cell.com/abstract/S0092-8674(10)00938-4)

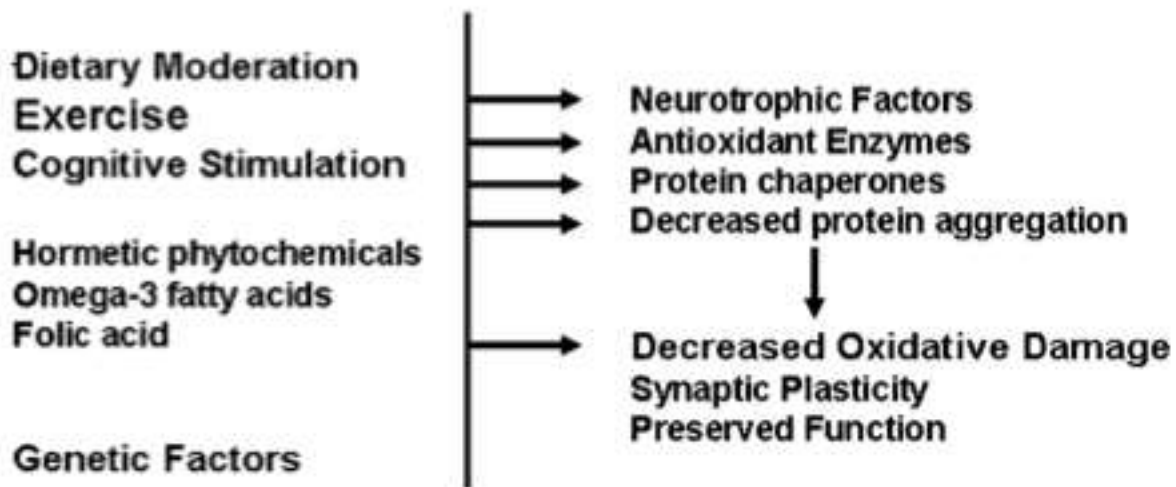
Roles of ATP

- Cu is ATPase (needs O₂ generated ATP)
- Cu is also ferroxidase (relieves neurons of iron and excess iron)
 - What uses ATP during cell function?
 - What happens when ATP not available via hypoxia?

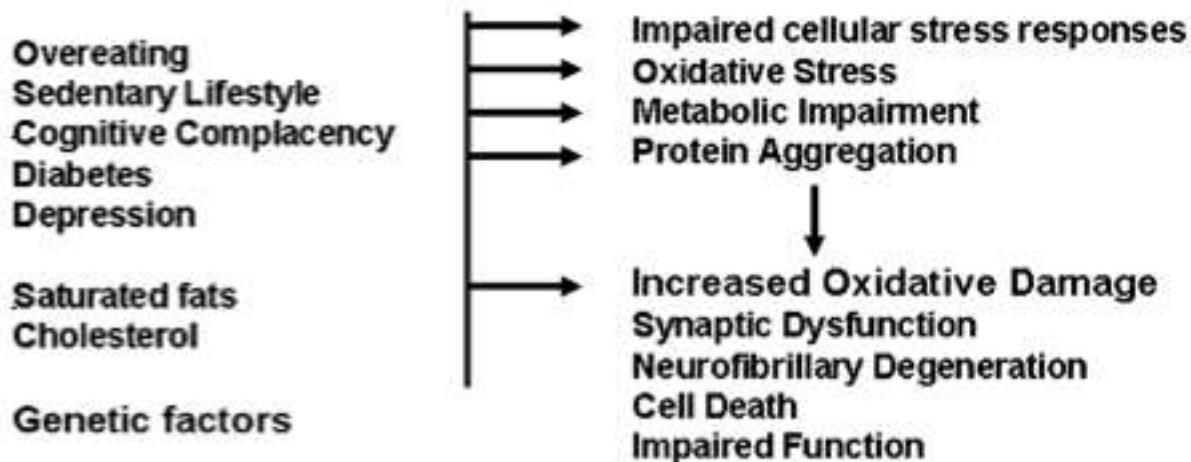
Plaques

- K center
- Fe, Zn and Cu surround
- Basic (high H arena) H-

Healthy Brain Aging



Neurodegenerative Disease



Diagnosis

- Chronic, progressive hypoxia leading to breakdown of mitochondria, ATP production, failure of copper transport to cell and iron export from cell.