Mitochondria and the production of ATP

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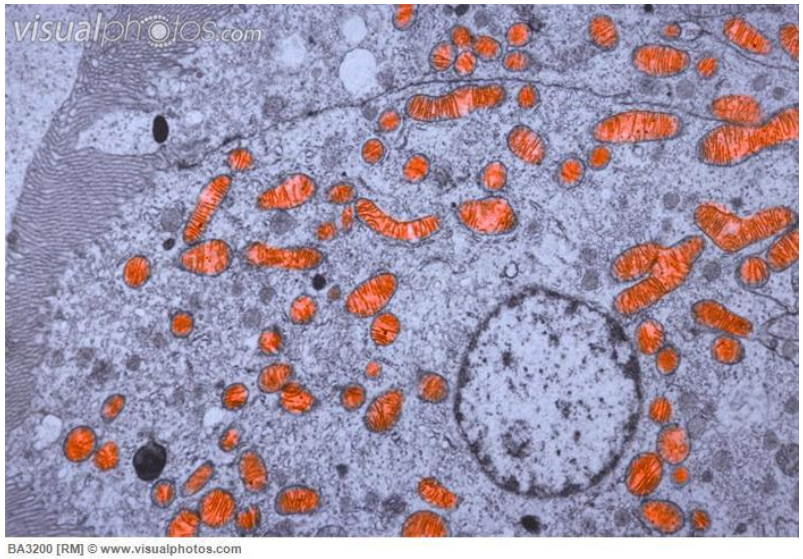
THE STRUCTURE OF MITOCHONDRIA

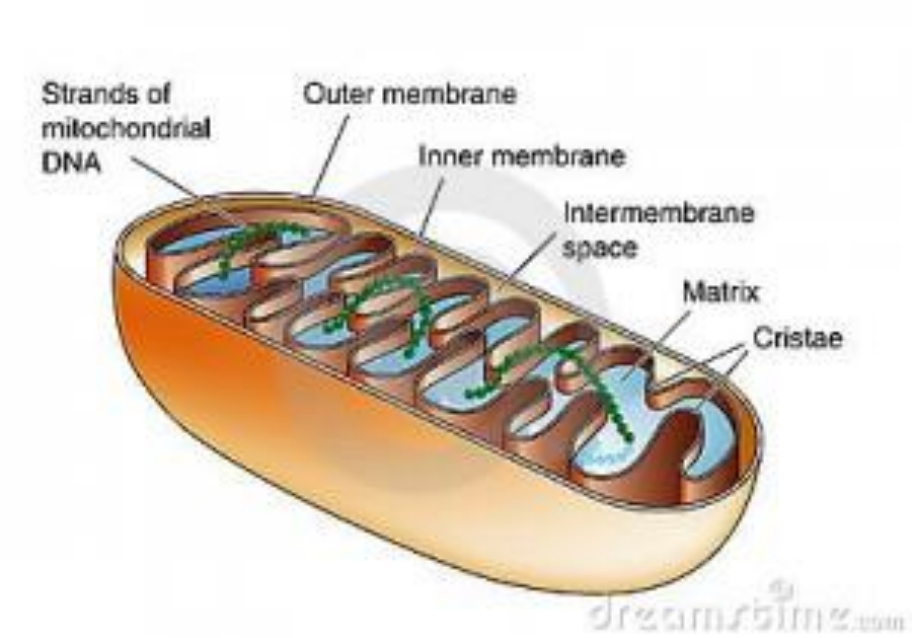
The mitochondrion

- Greek Mitos = „thread”, and chondrion = „granule”
- found in most eukaryotic cells
- „energy factory of the cell"
- 0.5 to 1.0 micrometer (µm)
- Number: 1- several thousand /cell



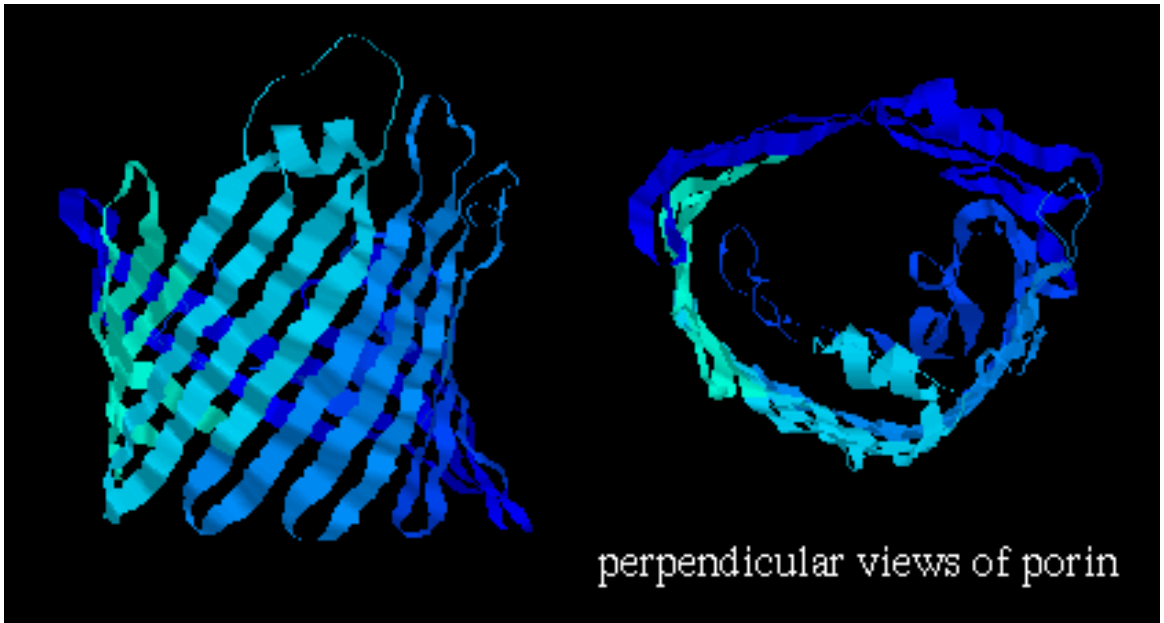
The mitochondrion

- Surrounded by a double membrane:
  1. Outher membrane
  2. Intermembrane space
  3. Inner membrane (cristae)
  4. Mitochondrial matrix

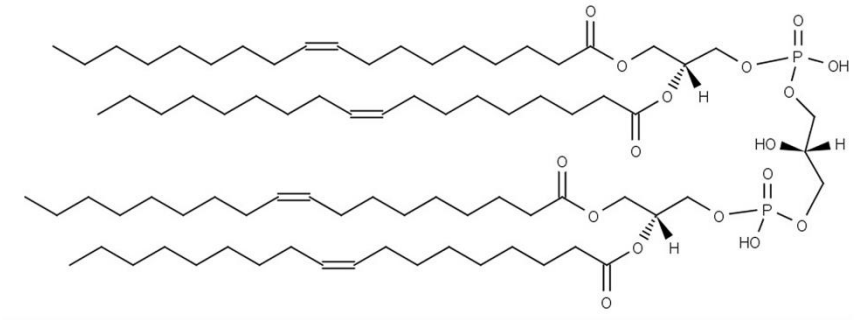


1. Outher membrane

- similar to the eukaryotic plasma membrane (protein:phospholipid = 1:1)
- Contain porin proteins → make the membrane permeable to 10.000 Dalton



2. Inner membrane

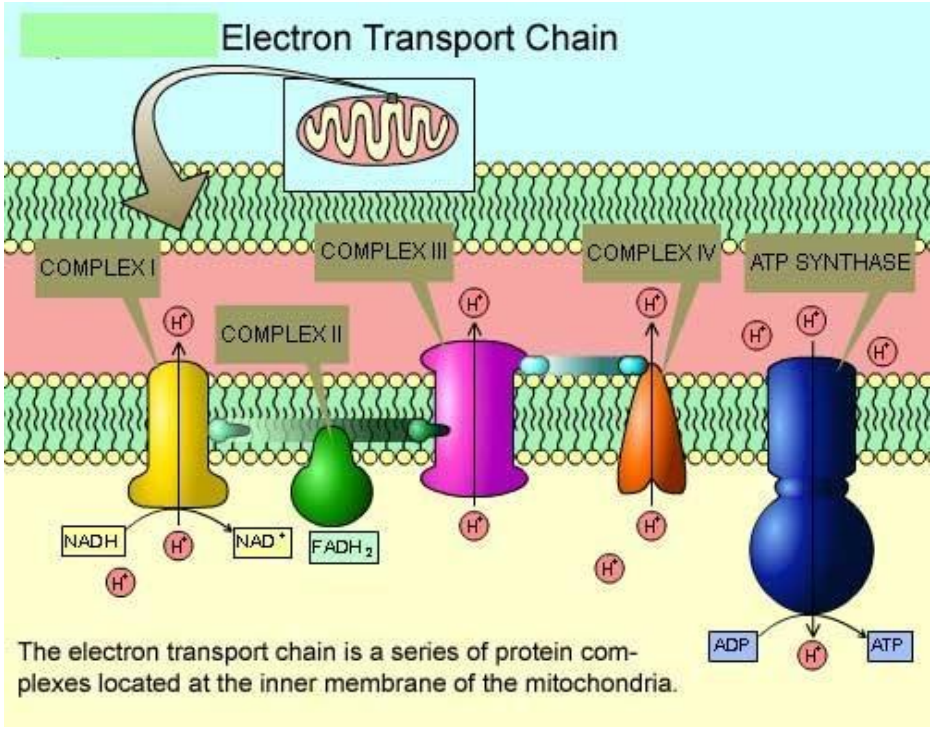


Cardiolipin
1',3'-Bis-[1,2-di-(9Z-octadecenoyl)-sn-glycero-3-phospho]-sn-glycerol

- protein:phospholipid = 80:20
- rich in cardiolipin (phospholipid) → makes the inner membrane impermeable
- molecules require special transport proteins to enter or exit the matrix
- forms cristae

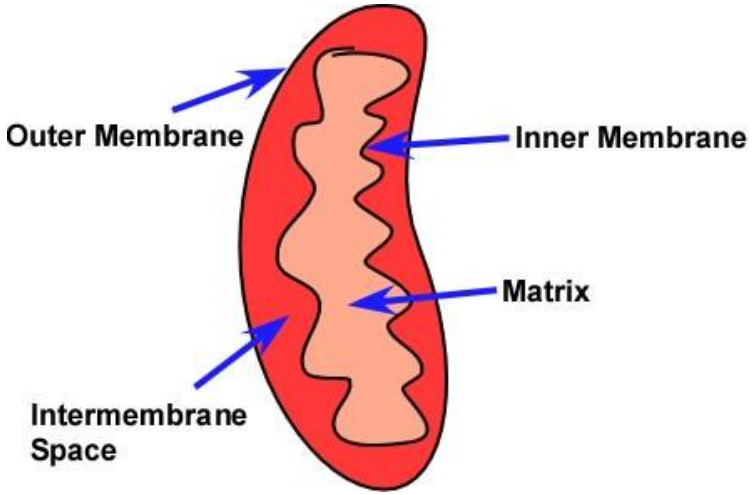
2. Inner membrane

- Cristae
  - expand the surface area of the inner mitochondrial membrane
  - Contain proteins:
    - Specific transport proteins
    - Proteins of the electron transport chain
    - ATP-synthase

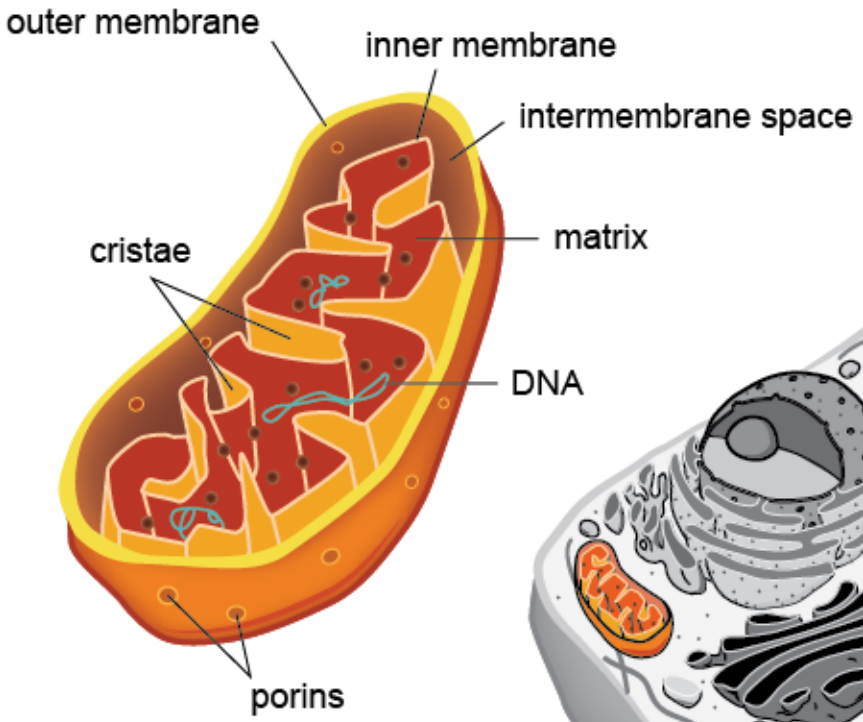


3. Intermembrane space

- Between the outer membrane and the inner membrane
- the concentrations of molecules in the intermembrane space is the same as in the cytosol



4. Matrix

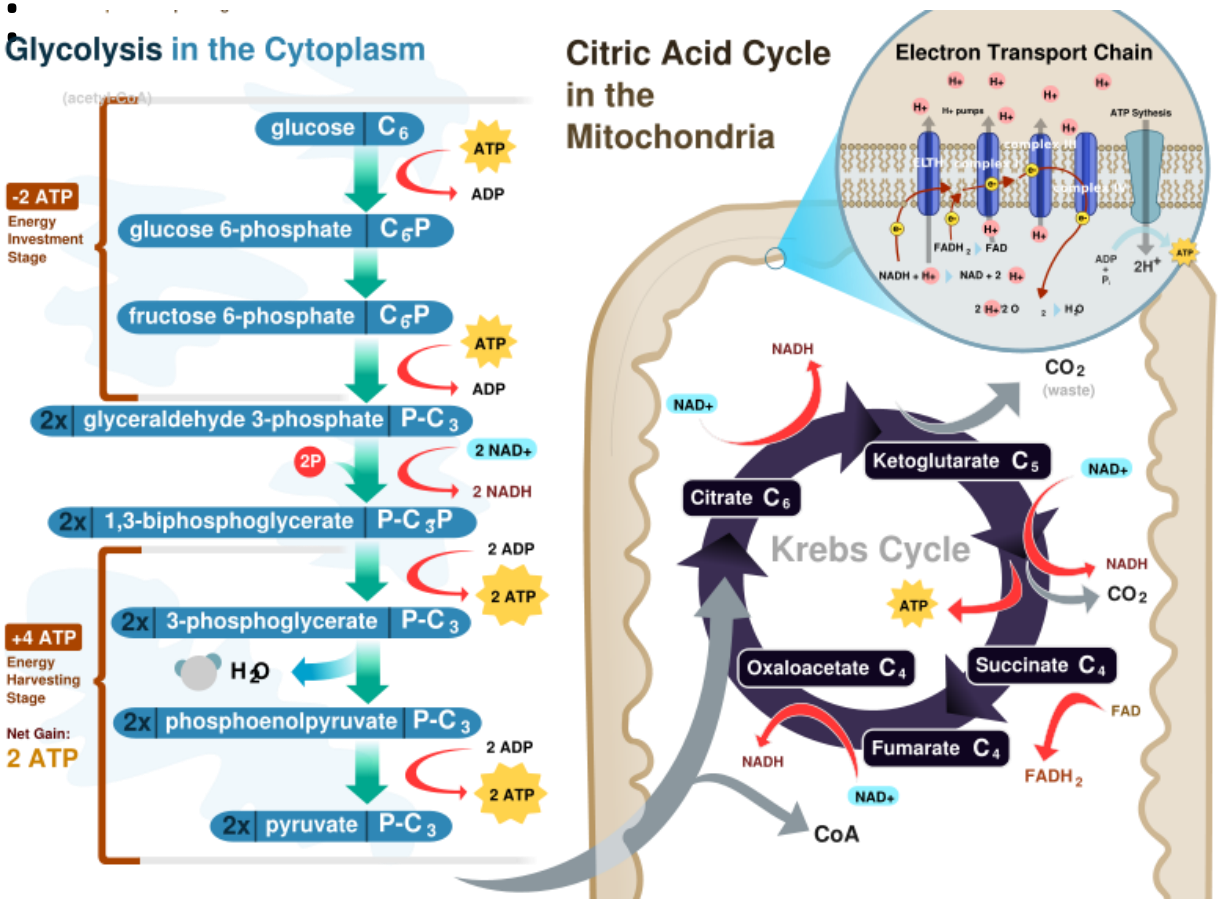


- Gel-like
- Contains:
  - hundreds of enzymes
  - special mitochondrial ribosomes, tRNAs and mRNAs
  - several copies of the mitochondrial DNA genome

THE SYNTHESIS OF ATP

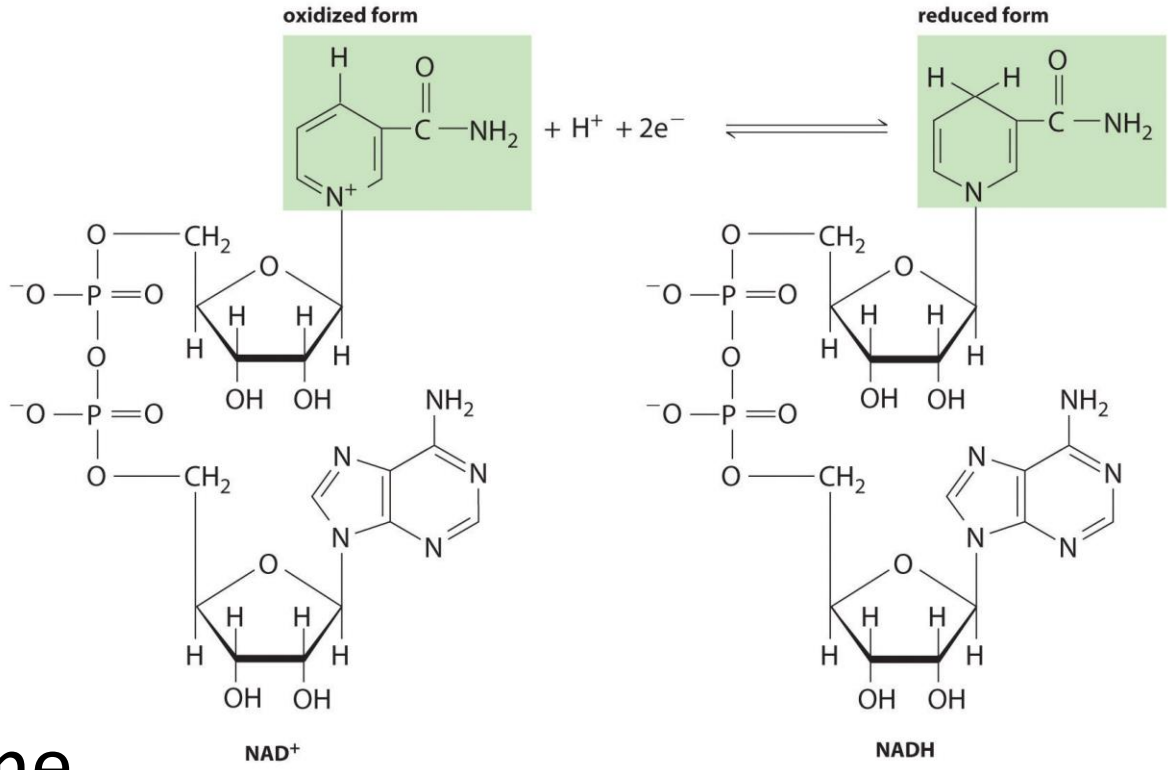
The synthesis of ATP

- From glucose and fatty acids
- 3 main processes:
  1. Glycolysis
  2. Citric acid cycle
  3. Terminal oxidation



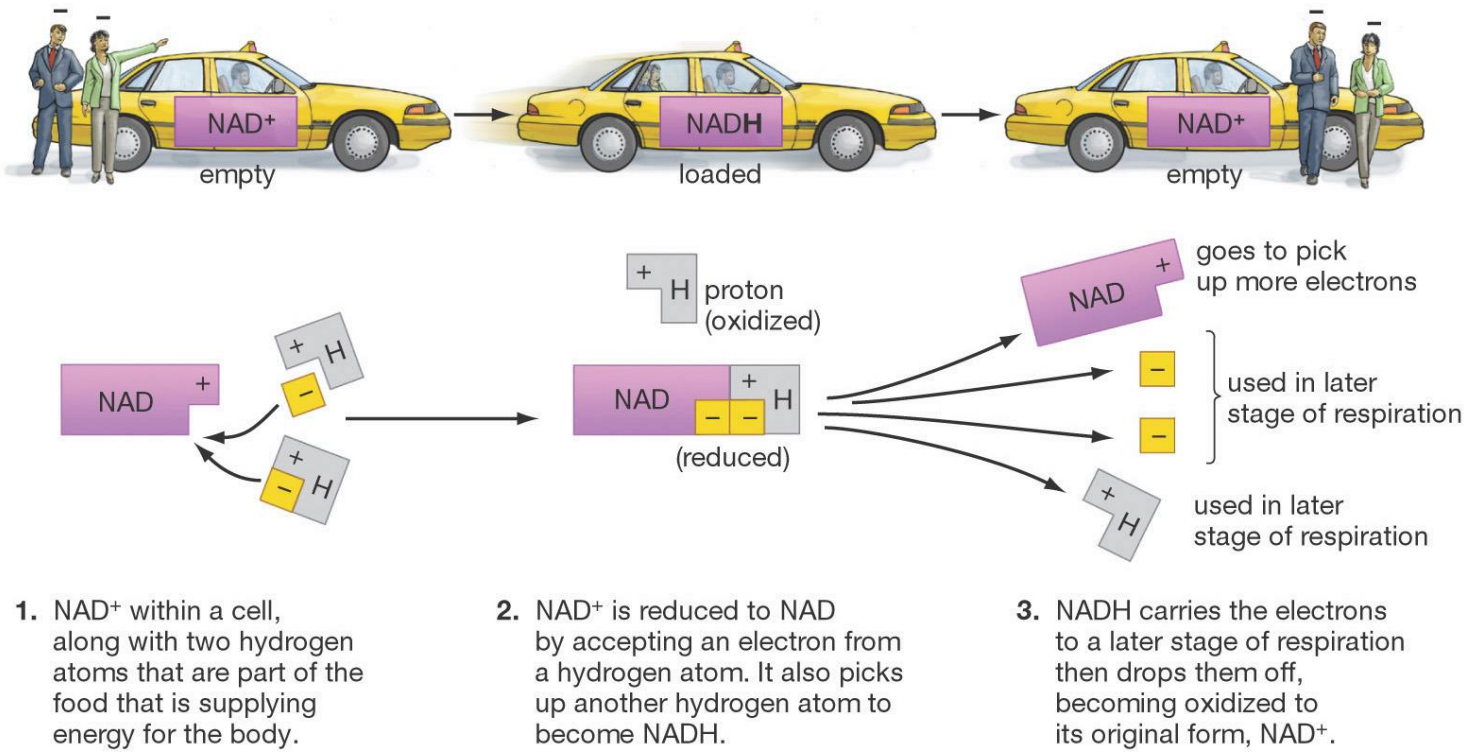
NAD^+

(Nicotinamide adenine dinucleotide)



- Coenzyme
- transports electrons from one reaction to another

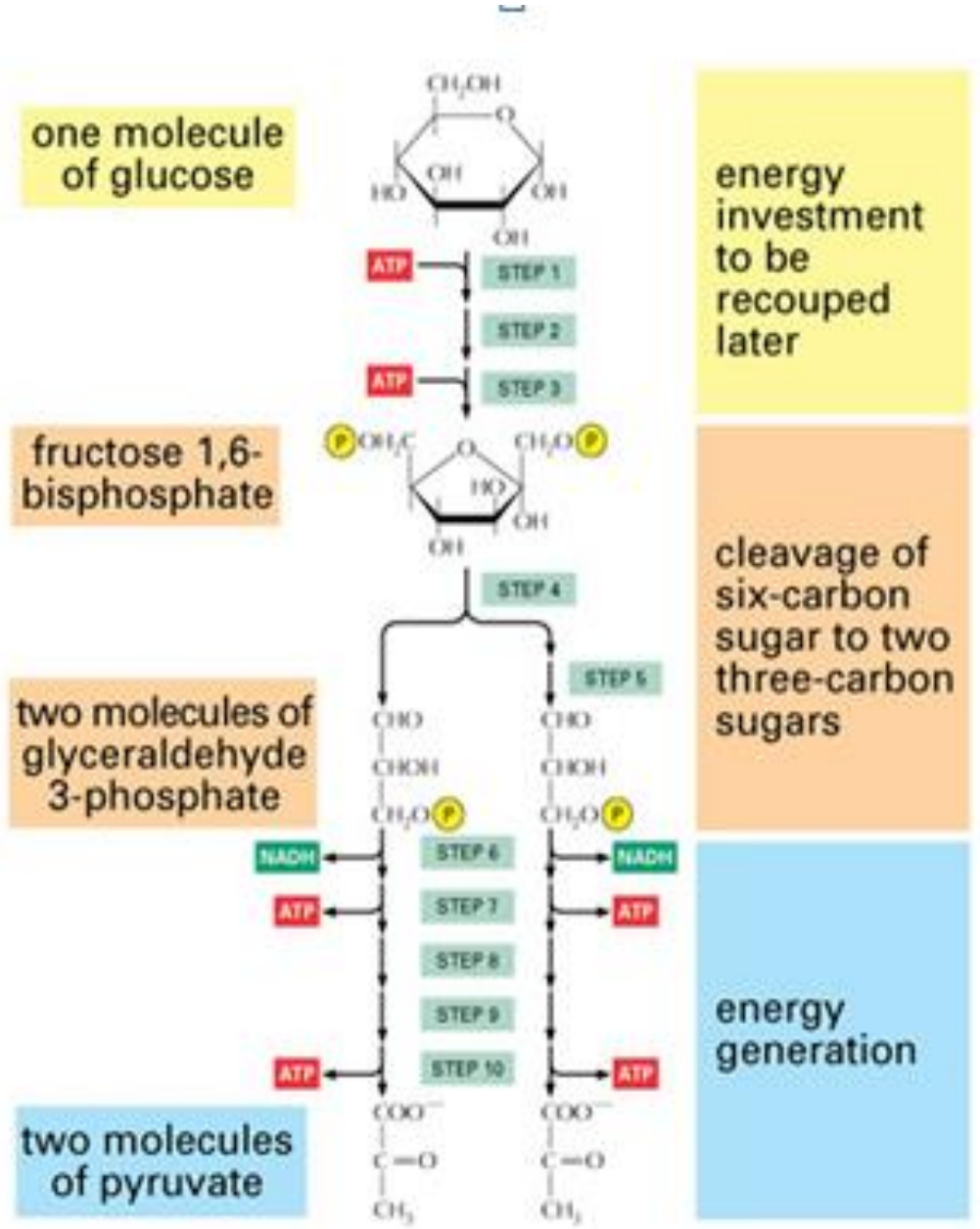
NADH (Nicotinamide adenine dinucleotide)



- NAD^+ → accepts electrons from other molecules and becomes reduced → NADH
- NADH → donate electrons and becomes oxidized to its original form → NAD^+

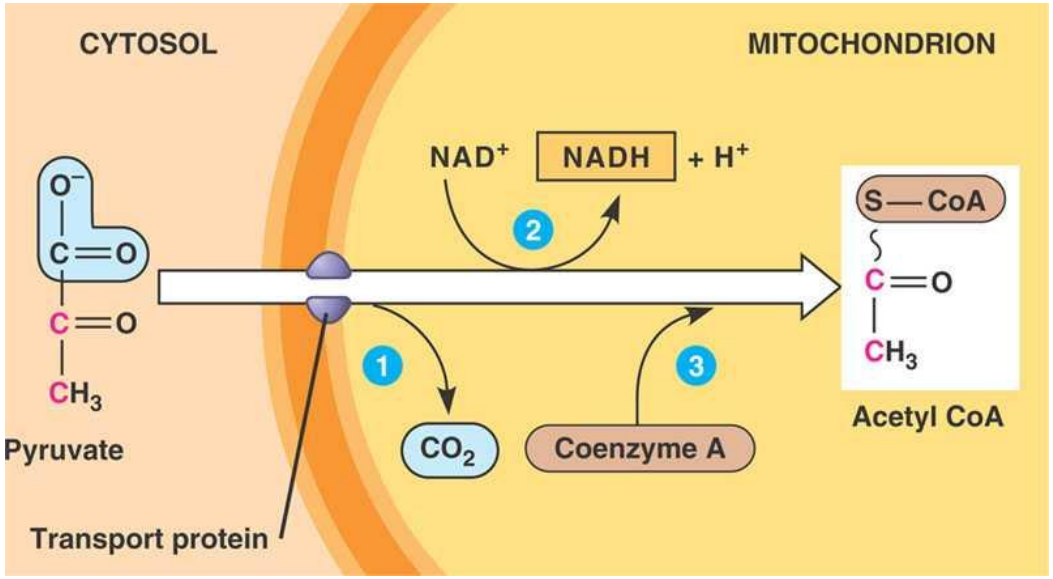
1. Glycolysis

- converts glucose (C_6) into pyruvate (C_3)
- in the cytosol
- oxygen is never involved in the reaction
- ten reactions → ten intermediate compounds
- formation of 2 ATPs (4-2) and 2 NADHs, 2 pyruvates



2. Citric acid cycle/ Szent-Györgyi and Krebs cycle

- in the matrix of the mitochondrion
- Pyruvate (C_3) loses 1 carbon atom → acetic acid (C_2)
- Acetic acid + Coenzyme A (CoA) → Acetyl CoA



2. Citric acid cycle/ Szent-Györgyi and Krebs cycle

- Oxaloacetate (C_4) + acetyl group (C_2) = citrate (C_6)

- Formation of:
  - 2 CO_2
  - 3 NADH
  - 1 $FADH_2$
  - 1 GTP

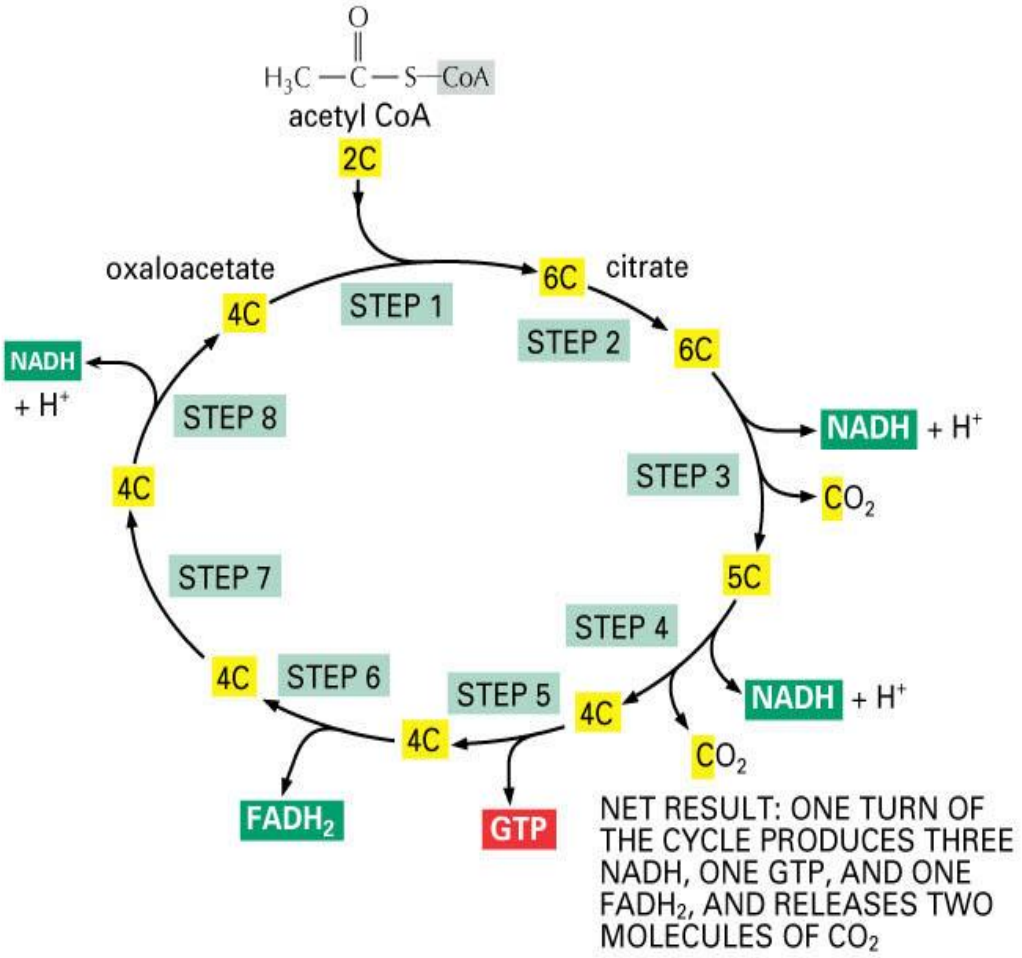
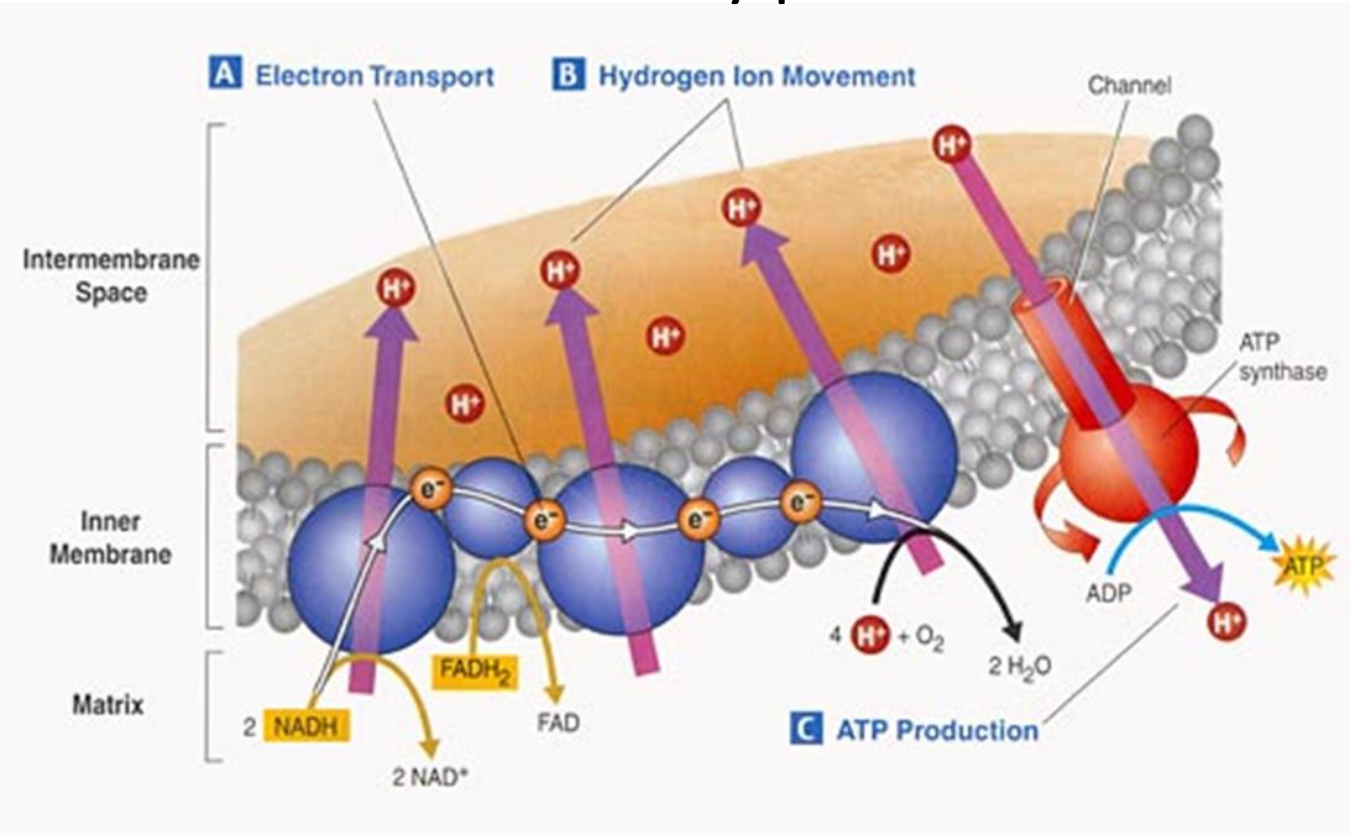


Figure 13-11 Essential Cell Biology, 2/e. (© 2004 Garland Science)

3. Terminal oxidation / Oxidative phosphorylation

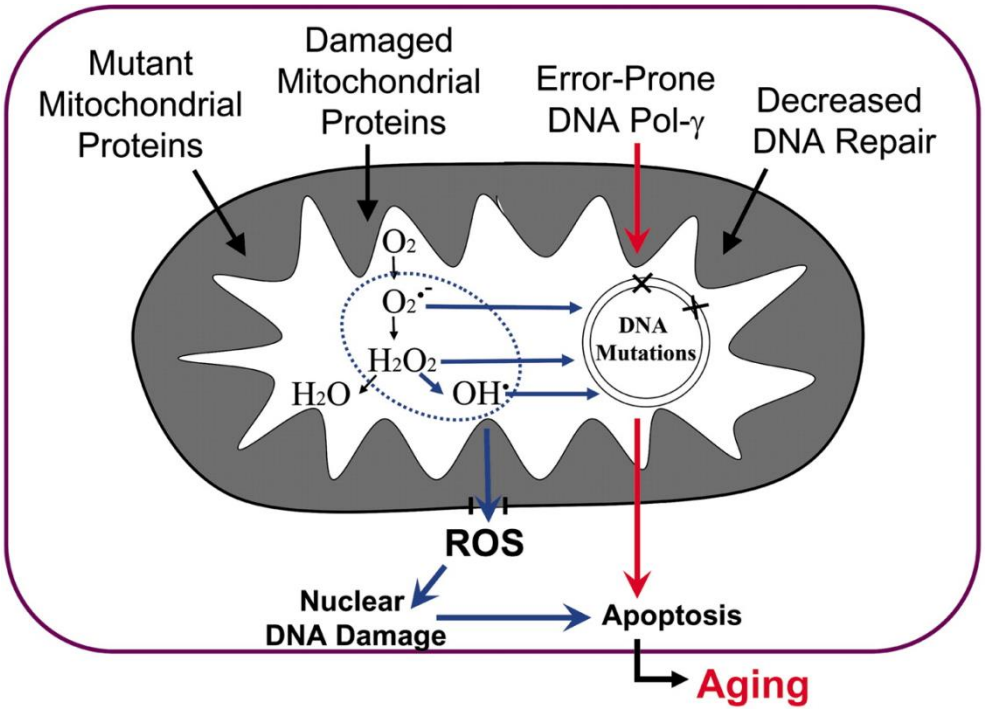
- In the inner mitochondrial membrane by protein complexes
- 3 events:
  a) Oxidation of coenzymes → transport of the electrons



The final electron acceptor is molecular oxygen → is reduced to water (harmful intermediates are generated =ROS)

Reactive oxygen species (ROS)

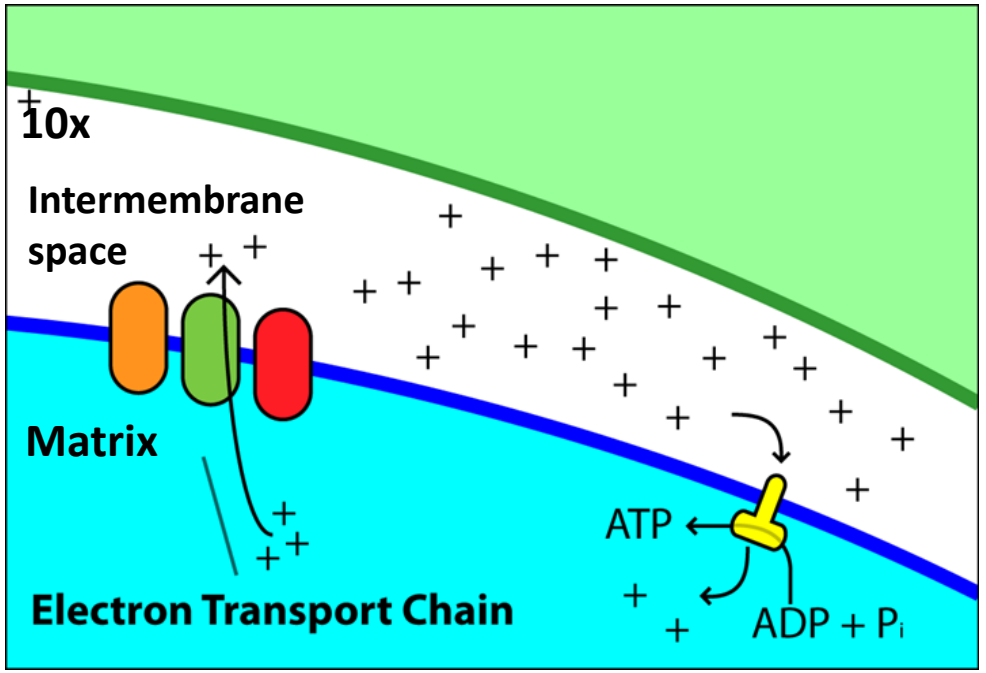
- During reduction of oxygen → harmful, instable intermediates are produced (superoxide or peroxide anions)
- These are called reactive oxygen species (ROS):
  - are very harmful to cells
  - oxidize proteins, destroy the membrane and cause mutations in DNA
  - Cause diseases and is proposed as one cause of aging



3. Terminal oxidation / Oxidative phosphorylation

b) Movement of protons:

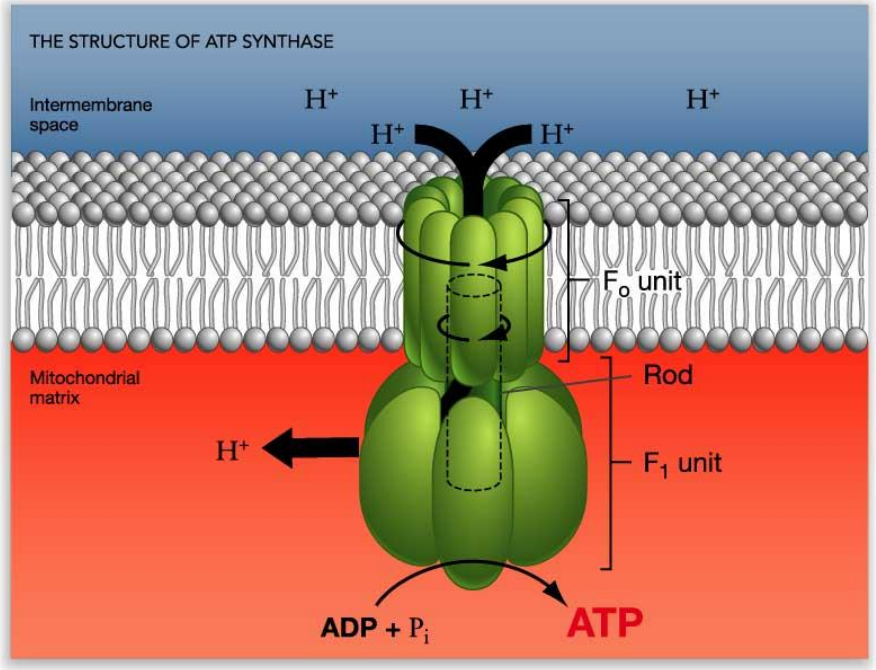
- Are pumped into the intermembrane space → electrochemical proton gradient (proton-motive force)
- Protons have to flow back into the matrix trough ATP synthase



3. Terminal oxidation / Oxidative phosphorylation

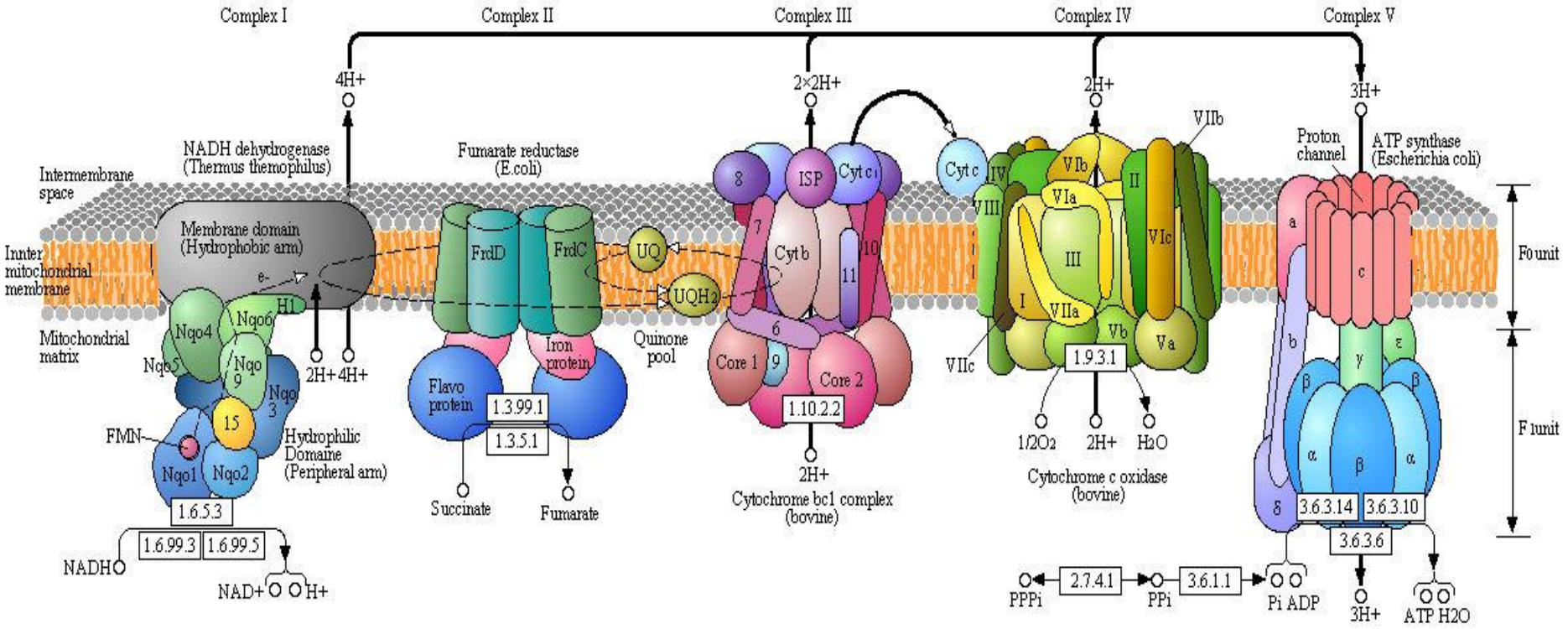
c) ATP synthesis by ATP sythase:

- Enzyme complex
- F_o: proton channel
- F_1: catalytic activity



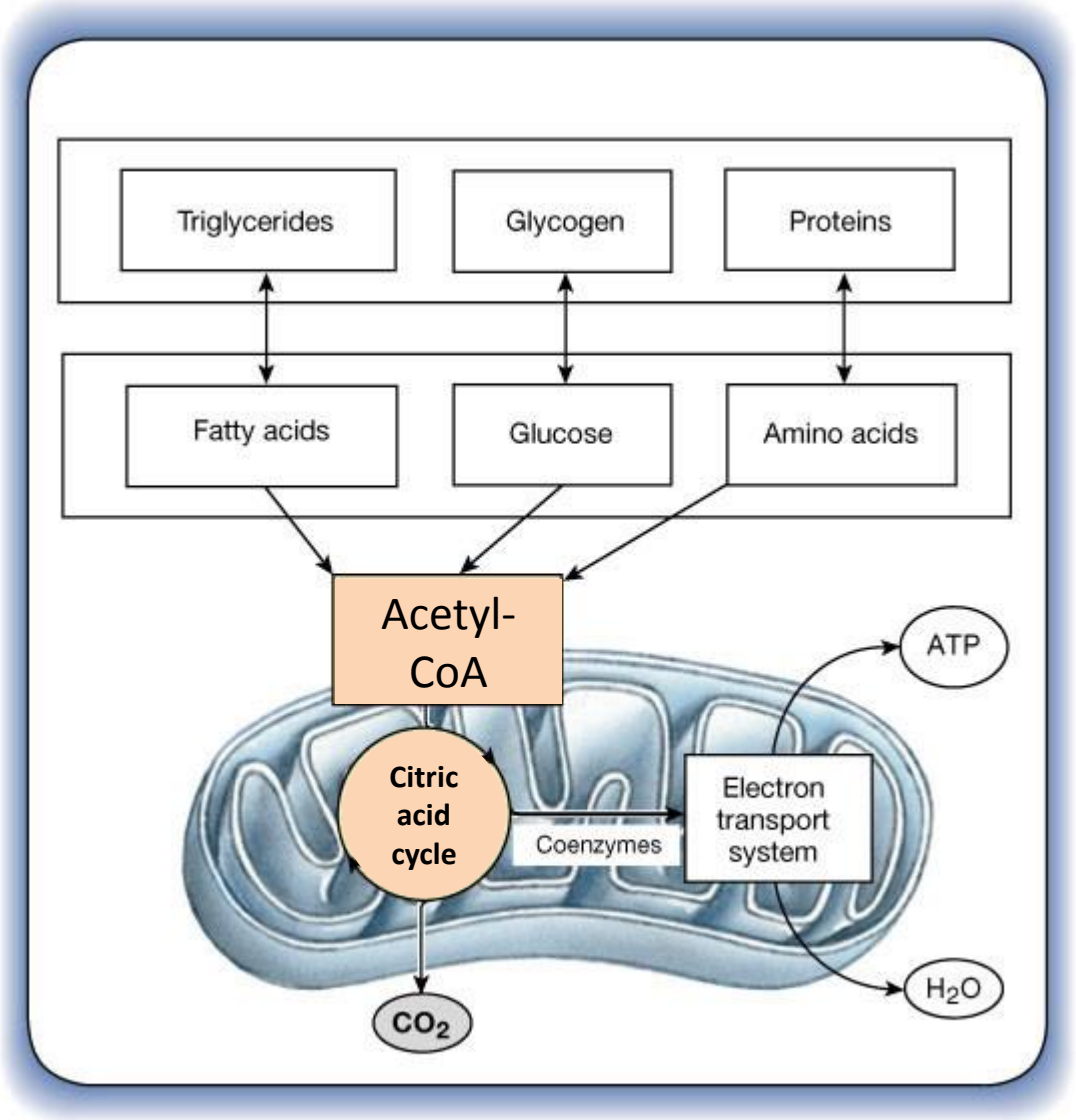
- Protons flow trough the complex (chemiosmosis) → this kinetic energy rotates the F_1 subunit → synthesis of ATP from ADP + P_i

Subunits of the electron transport chain



ATP production from bioorganic molecules

- 1 g fatty acid: 9Kcal/37kJ
- 1 g carbohydrate: 4Kcal/17kJ
- 1 g protein: 4Kcal/17kJ



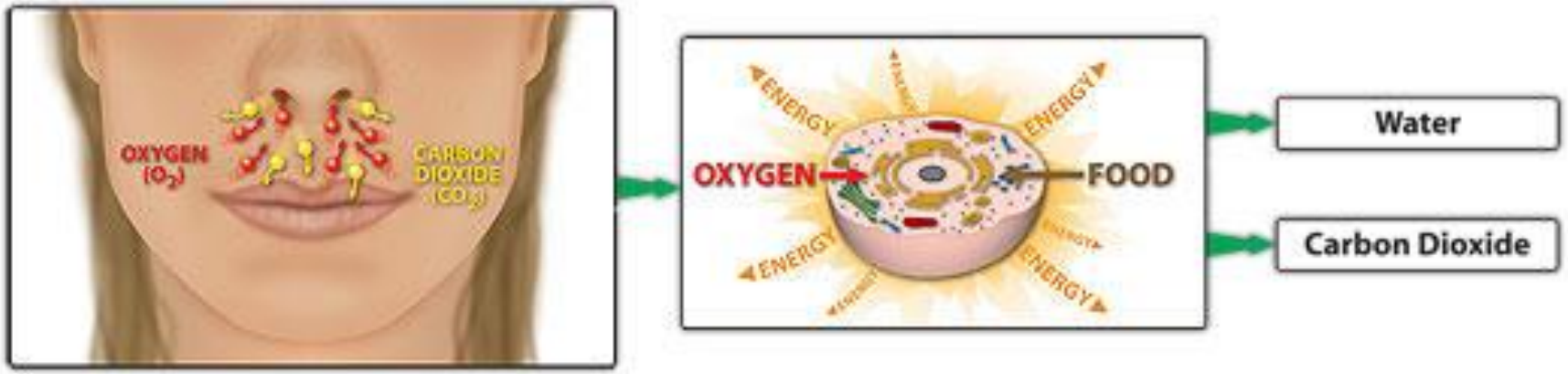
Fully oxidation of 1 glucose molecule into CO_2

- Glycolysis:
  - Production of 4 ATP but 2 are consumed → 2 ATP
- Citric acid cycle:
  - 2 ATP (indirectly)
- Oxidative phosphorylation:
  - 30 or 32 ATP

→ 34 or 36 ATP molecules

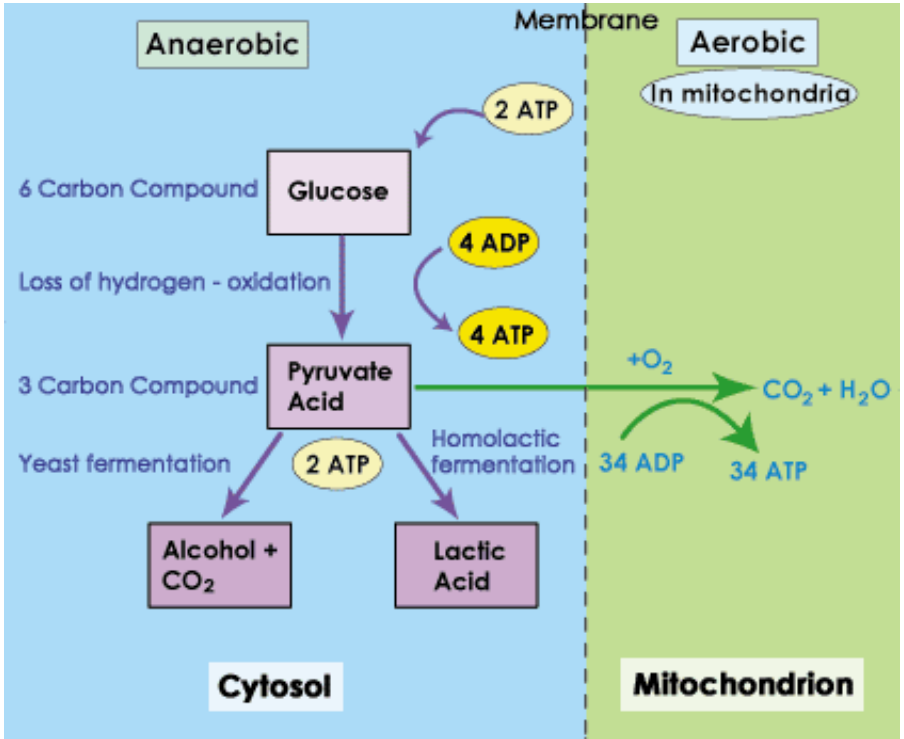
Aerobic organisms

- requires oxygen to grow
- use oxygen to make energy (cellular respiration)
- Produce more energy than anaerobes ↔ high levels of oxidative stress



Facultative anaerobic organisms

- make ATP by aerobic respiration if oxygen is present
- switch to <u>fermentation</u> if oxygen is not present



Additional functions

Mitochondria play a central role in many other metabolic tasks:

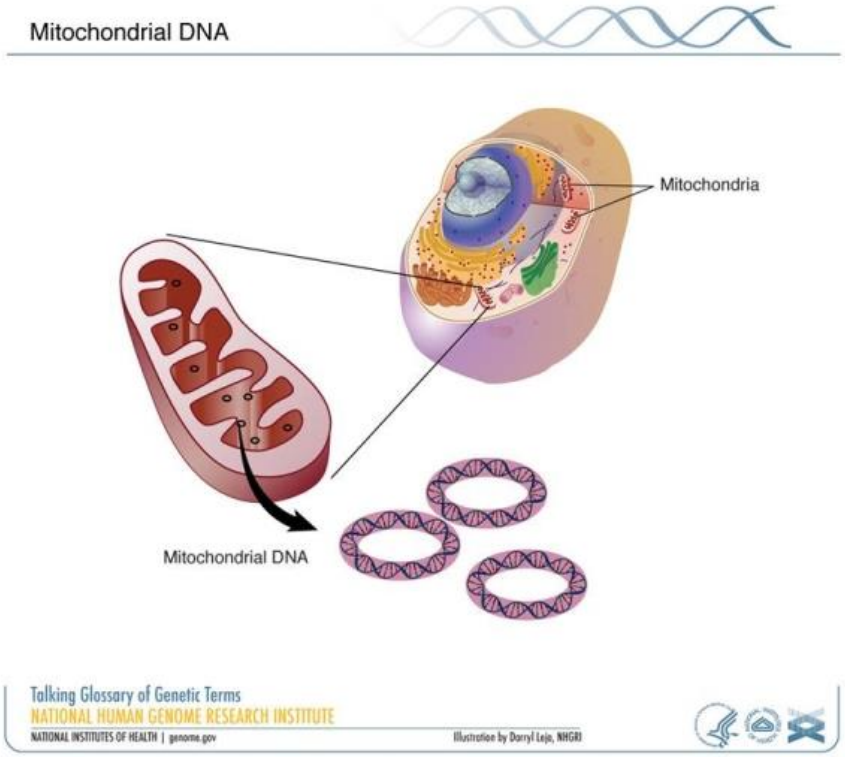
- Regulation of the membrane potential
- Apoptosis (programmed cell death)
- Signaling (regulation of gene expression)
- Regulation of cellular metabolism
- Steroid synthesis
- …

→ mutation in the genes regulating any of these functions can cause mitochondrial diseases

GENETIC APPARATUS OF MITOCHONDRIA

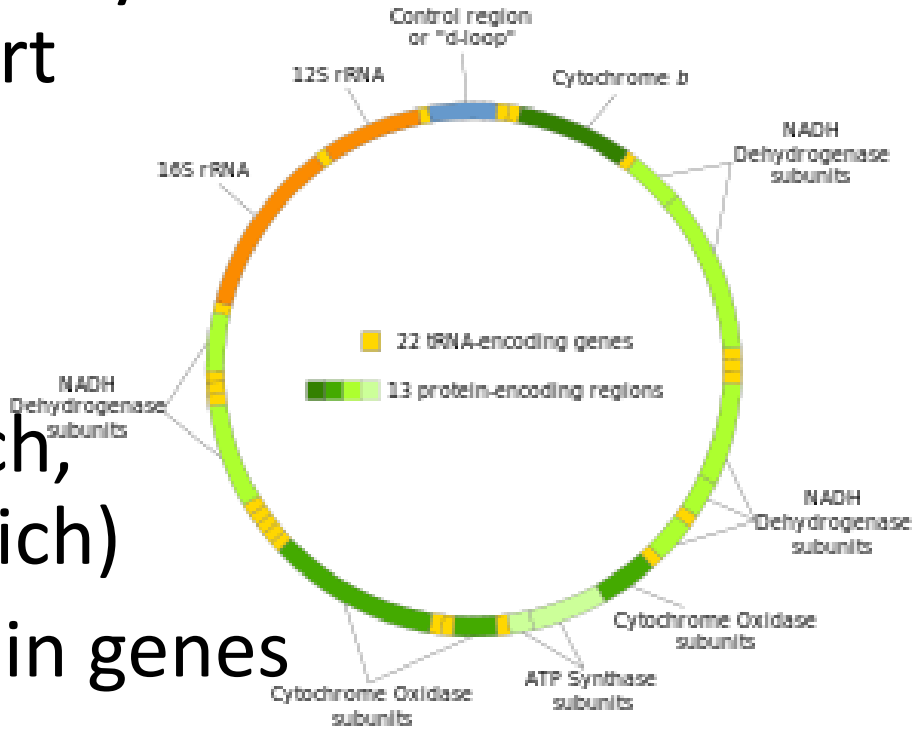
Mitochondrial DNA

- 2-10 mtDNA copies/mitochondrion
- Double stranded, circular, short (~16,600 base pairs)



Mitochondrial DNA

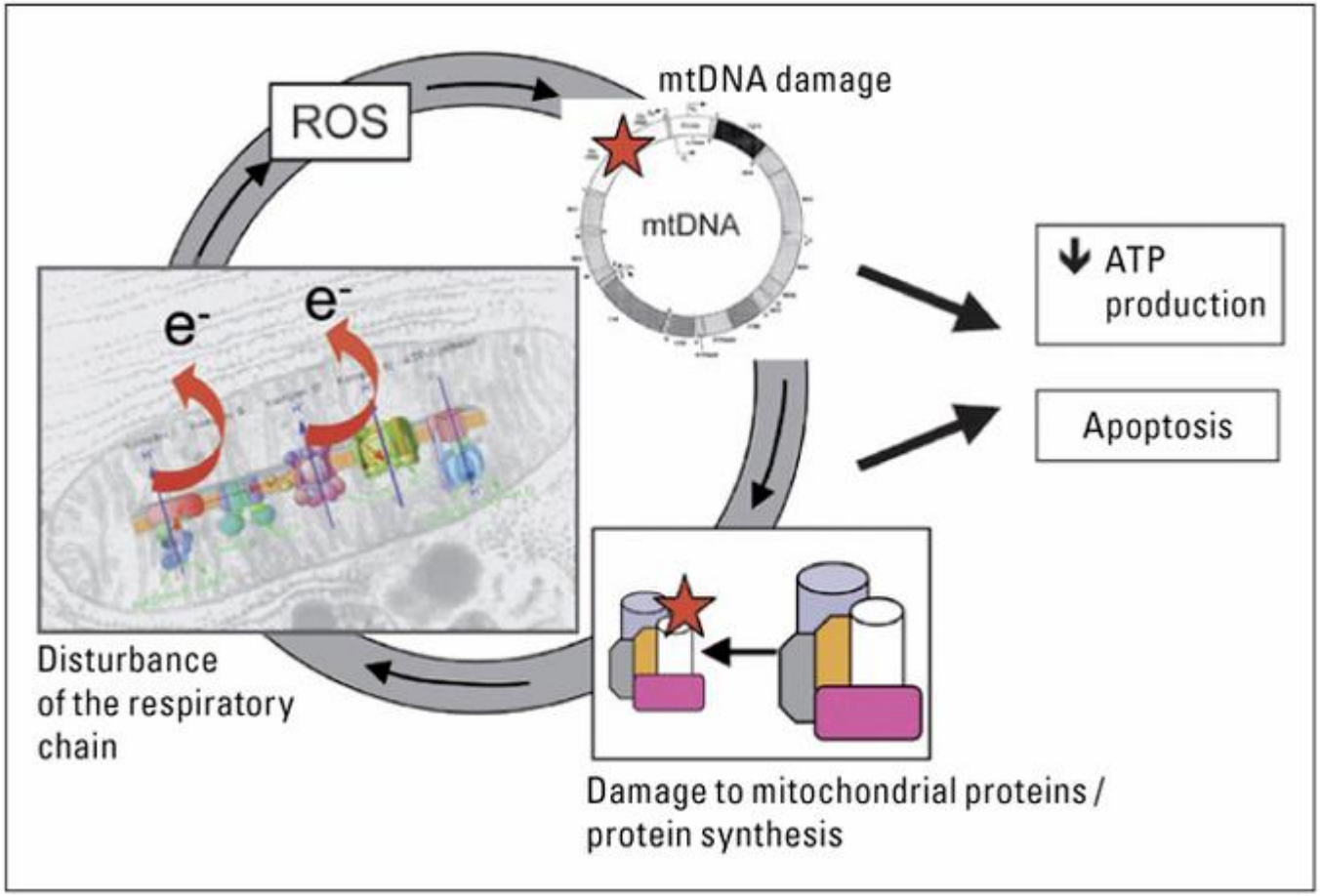
- Codes for only 37 genes (13 for proteins, 22 for tRNA and 2 for rRNA)
- other genes are in the eukaryotic nucleus → posttranslational transport
- the two strands are different by their nucleotide content (one strand is guanine-rich, other strand is cytosine-rich)
- both of the strands contain genes



Mutation of mtDNA

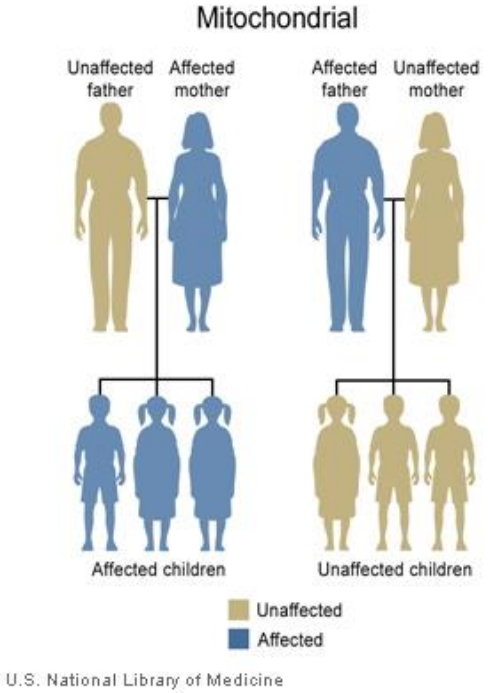
- Free radicals
- No histon proteins
- Proofreading and repair are weak

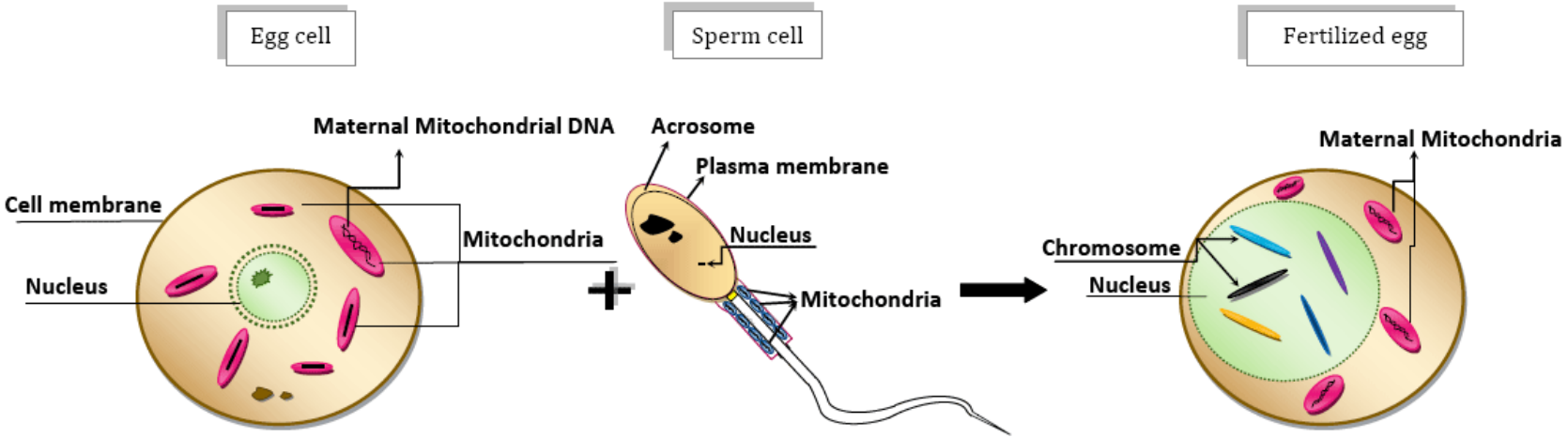
→ damage of the DNA, proteins and of the inner membrane



Inheritance of mitochondria

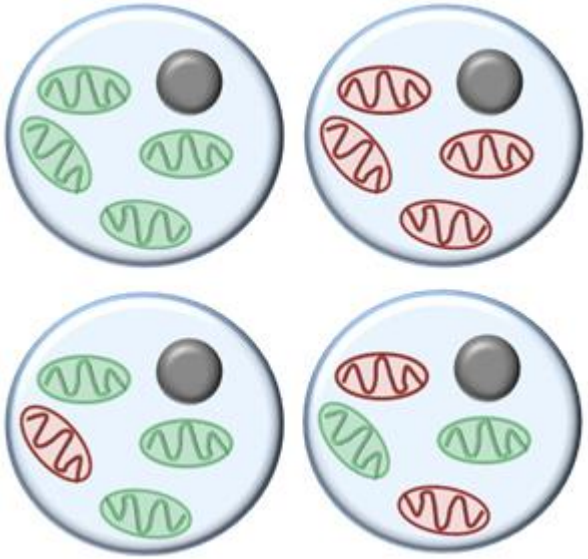
- Non- mendelian inheritance
- maternal inheritance
  (from mother to child)





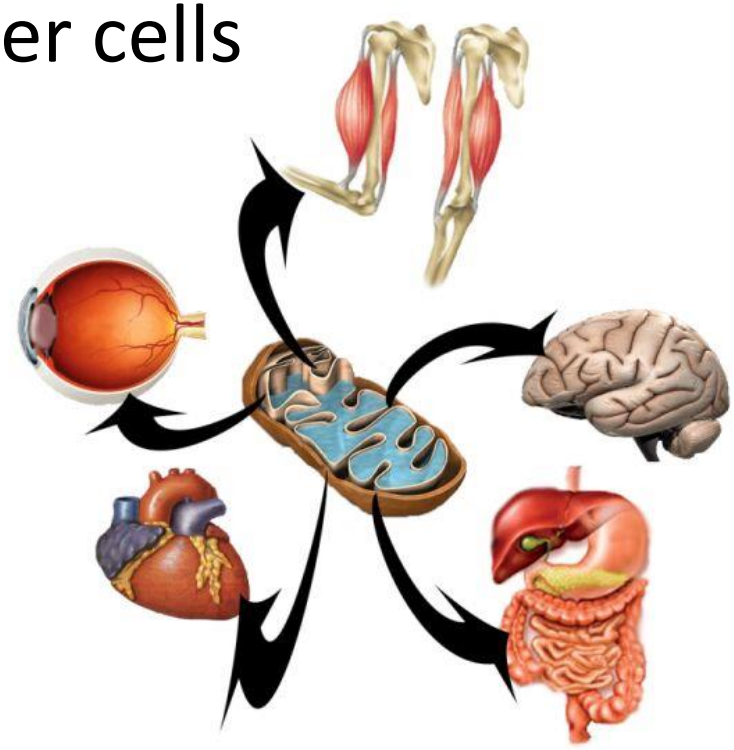
Inheritance of mitochondria

- Homoplasmy-copies of mtDNA are all identical in a cell (normal or mutated)
- Heteroplasmy- copies of mtDNA are different in a cell (normal and mutated)
  -ratio of mutated mtDNA
  reaches a treshold → disease



Mitochondrial diseases

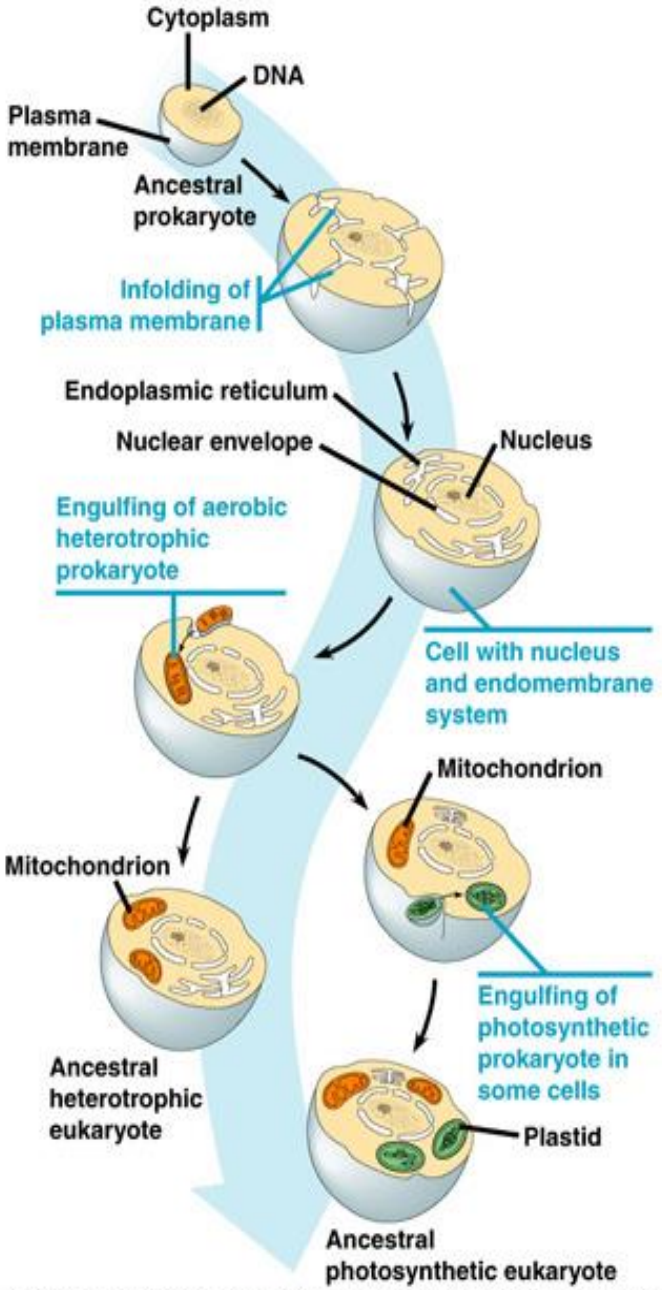
- Sensory organs, muscle, heart, nervous system, pancreas,… are affected → these cells use more energy than other cells
- neurological disorders
- Diabethes mellitus
- blindness
- myopathy (muscular weakness)



Endosymbiotic theory

- describes the development of eukaryotic cells
- Greek: endon = within, syn = together and biosis = living
- Konstantin Mereschkowski (1910)
- several cell organelles of eukaryotes originate from unicellular organisms

1. infolding of cell membrane → „compartments”
2. engulfing of prokaryotes → mitochondrion, plastids



Evidences

- formation of new mitochondria and plastids through binary fission
- both mitochondria and plastids contain single circular DNA that is similar to that of bacteria (most of their genes are transferred to the host cell genome)
- ribosomes are like those found in bacteria
- comparison of the genome
- …