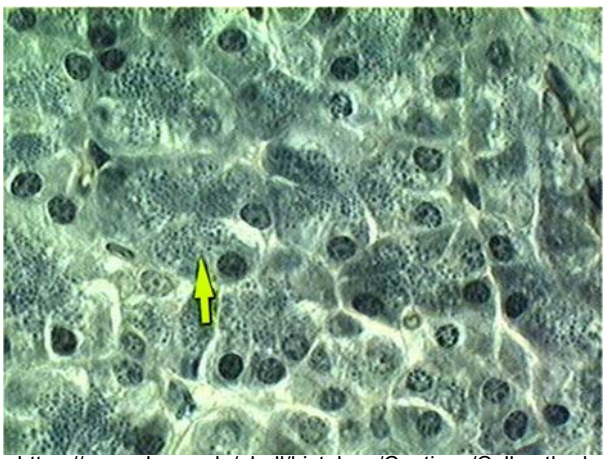
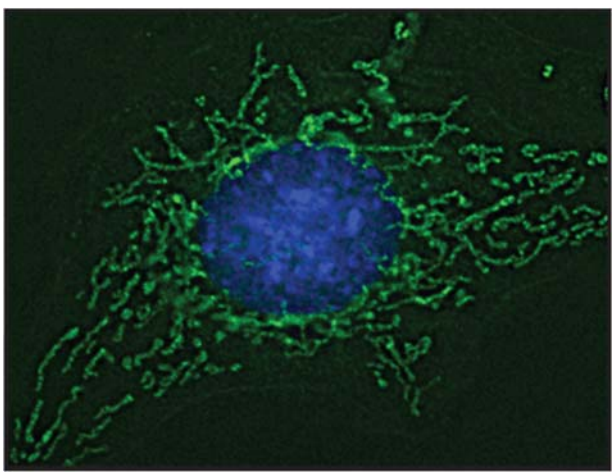
The Mitochondrion

- ***Definition***
- ***Structure, ultrastructure***
- ***Functions***

- Organelle definition
- Etymology of the name
  - Carl Benda (1903): μιτος (***mitos***) – thread; χονδριον (***khondrion***) – granule.
- Light microscopy identification
  - First time identified by Richard Altmann (1890);
  - Regaud's iron haematoxylin – black granules;
  - Janus Green B –vital stain (Leonor Michaelis, 1900);
  - Currently – Mito Tracker staining.

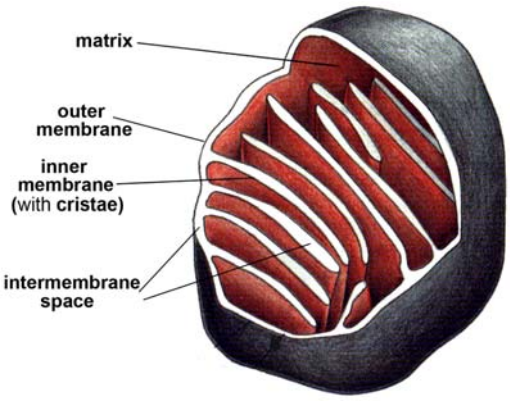


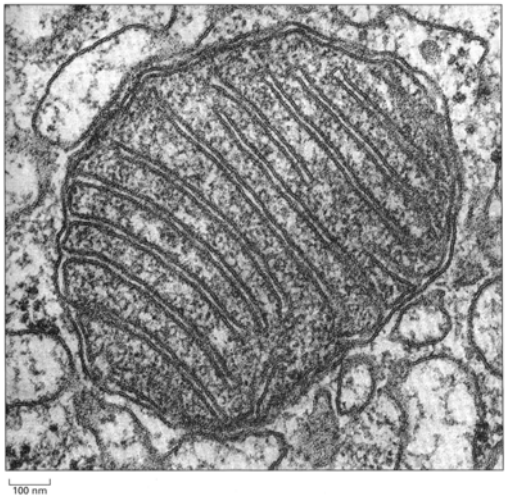
https://casweb.ou.edu/pbell/histology/Captions/Cellmethods/101.mitoch.ih.100x.html

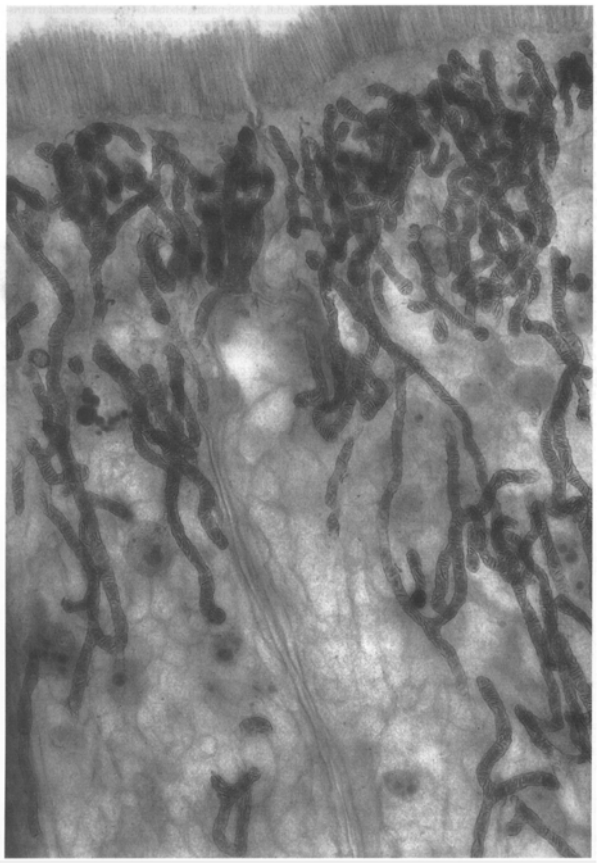


http://mcb.asm.org/content/33/20.cover-expansion

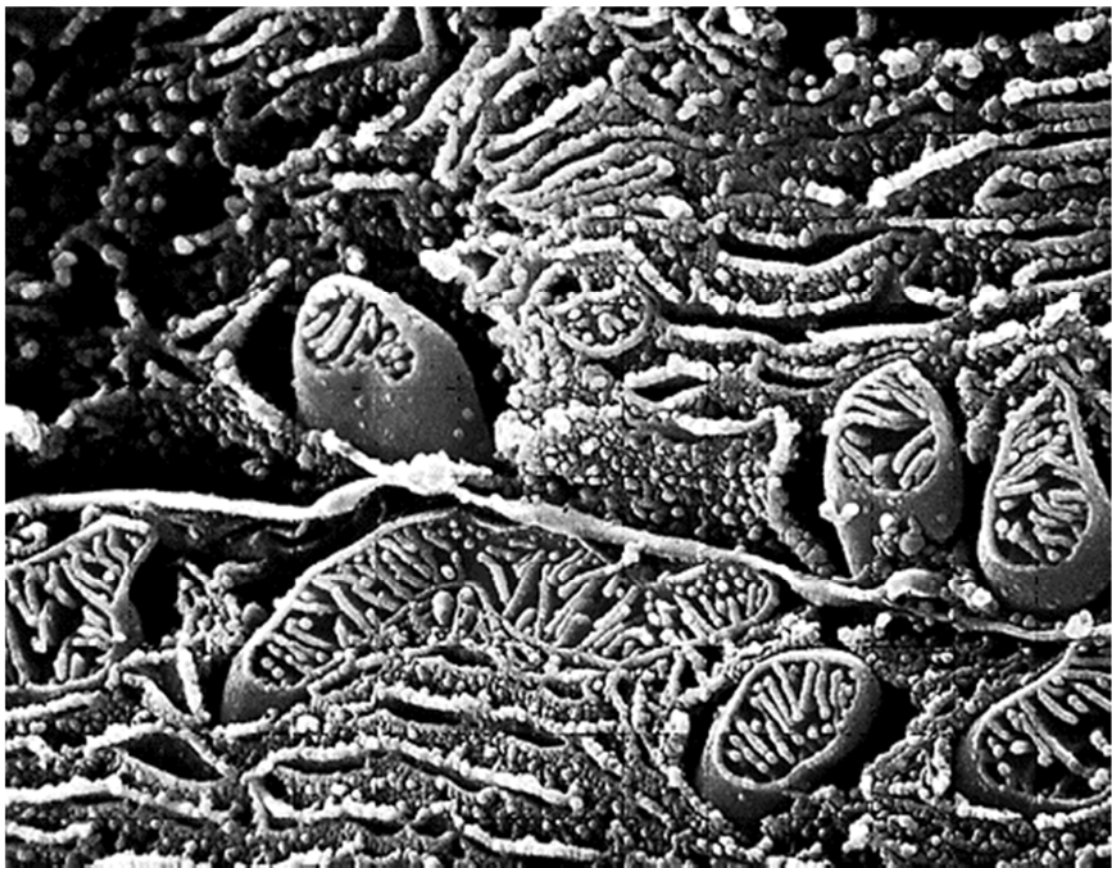
Mitochondrion ultrastructure *(i)*



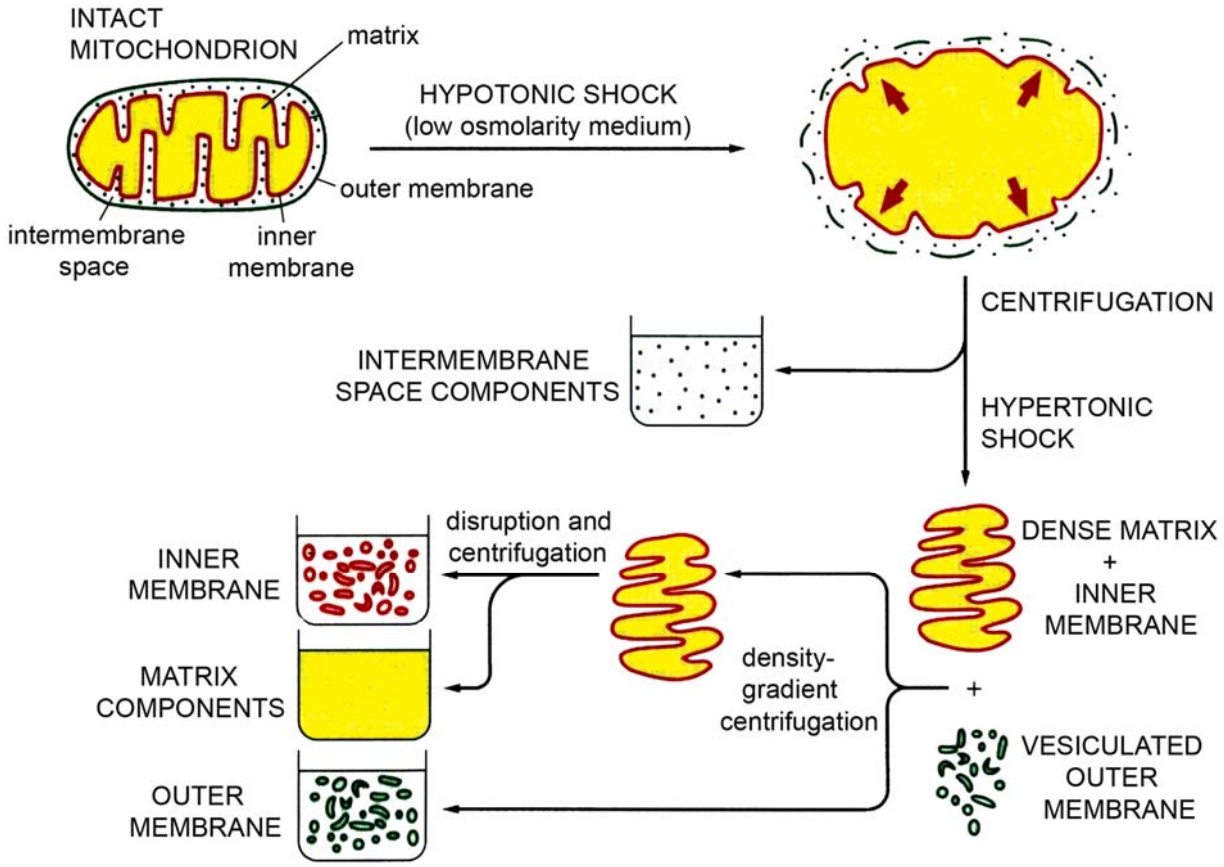




Mitochondrion ultrastructure *(ii)*



Experimental approach



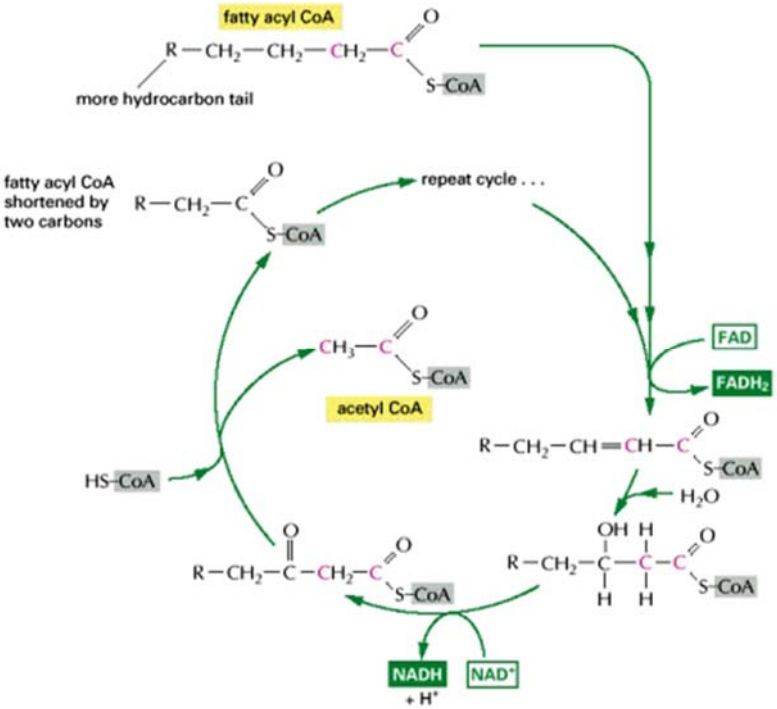
Mitochondrion functions *(i)*

- Functions of mitochondrial outer membrane
  - Controlled permeability (porins)
  - Acyl-CoA synthase
  - Carnityl-acyl-transferase I
  - Biogene amine inactivation (monoamineoxidase)
- Functions of intermembrane compartment
  - Buffer compartment (microclimate adequate for mitoplast function)
  - Adenylate-kinase (ATP + AMP = 2ADP)
  - Nucleoside phospho-kinase

Mitochondrion functions *(ii)*

- Functions of mitochondrial matrix
  - Citric acid cycle (tricarboxylic acid cycle, Krebs cycle)
  - β-oxidation of fatty acids (fatty acid oxidation cycle)
  - Protein biosynthesis
  - Mitochondrial DNA replication and transcription
- Functions of mitochondrial inner membrane
  - Transport of metabolites
  - Oxidative phosphorylation
    - Electron transport chain (respiratory chain)
    - ATP synthesis
  - Coupling of respiratory chain with ATP synthesis

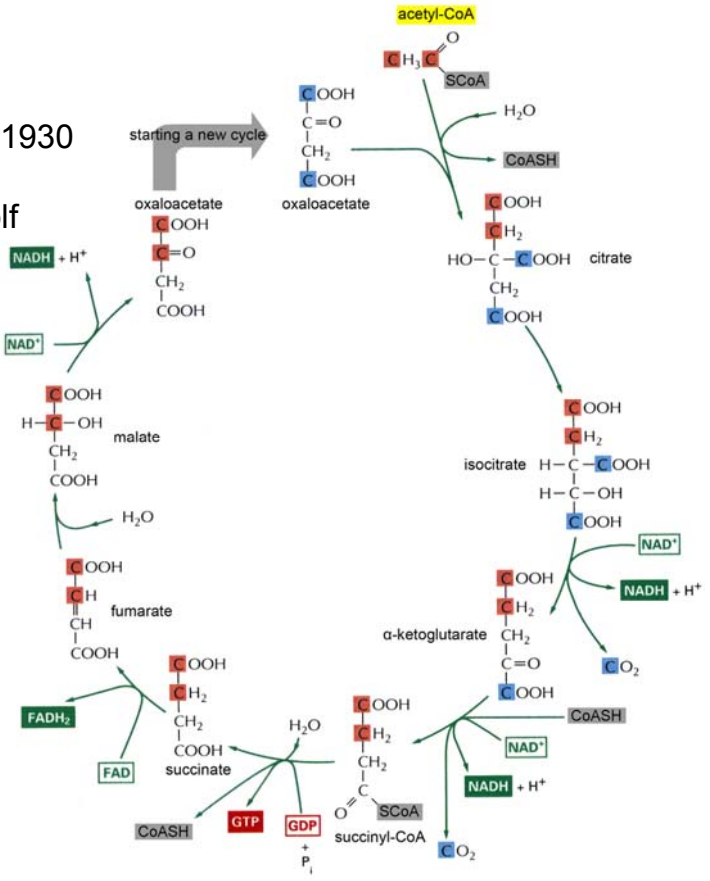
The fatty acid oxidation cycle



A cycle with 4 steps, producing:
- Acetyl-CoA – raw material for Kerbs cycle
- $FADH_2$ and NADH – raw materials for respiratory chain

Tricarboxylic acid cycle

First reactions of the cycle described in 1930 by Albert Szent-Györgyi
Finally deciphered in 1937 by Hans Adolf Krebs

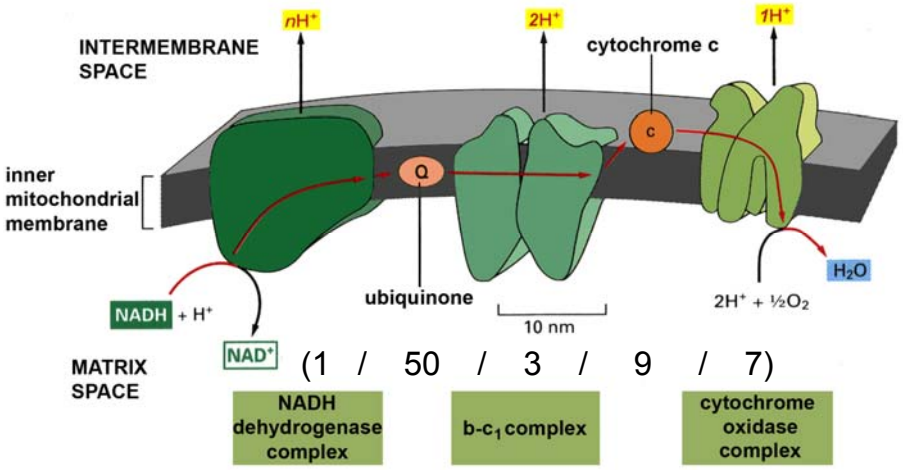


A cycle with 8 steps

Each step produces:

- 2 CO_2 molecules – waste products
- 3 NADH and 1 $FDAH_2$ molecules
- 1 GTP molecule and 1 released CoA

Respiratory chain



1. Complex I (NADH dehydrogenase caomplex)

- >900 kD
- >40 proteins (7 autonomous)
- 1 flavin center
- At least 7 iron-sulfur centers
- Takes up e^- from NADH lowering their energy and passing them to ubiquinone (CoQ)

2. Complex II (cytocrome b-c_1 complex

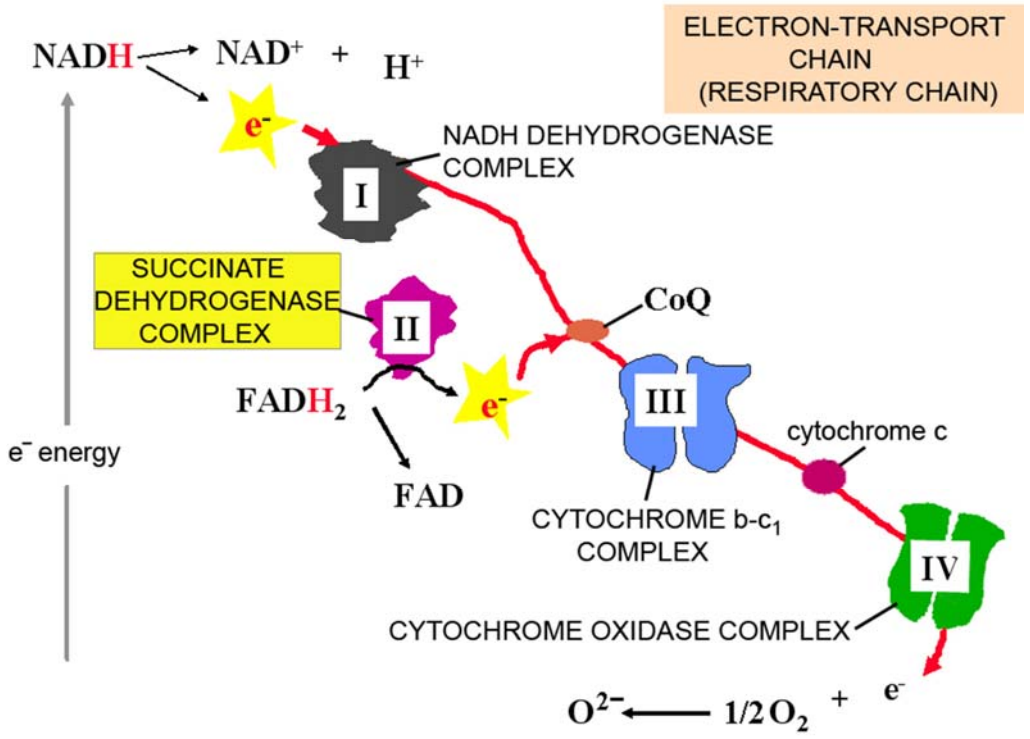
- ~240 kD
- at least 11 proteins (one autonomous)
- Acts as a dimer (2x240 kD)
- 3 heme centers; 1 iron-sulfur center
- Transfers e^- form CoQ to cytochrome c

3. Complex III (cytochrom oxidase or cytochrome a-a_3 complex)

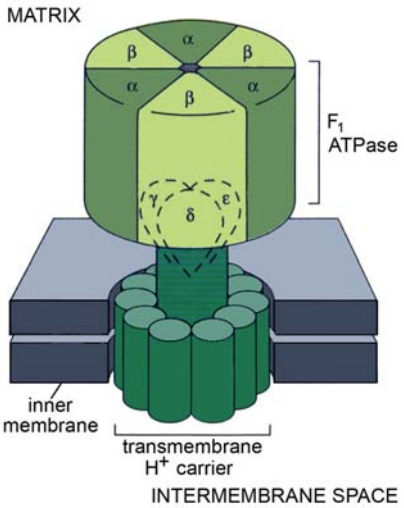
- 204 kD
- 13 proteins (3 autonomous)
- acts as a dimer (2x204 kD)
- 2 cytochroms, 2 centers with Cu^{2+} (bimetallic iron-copper centers)
- Transfers e^- from cytochrome c to oxygen, yielding water

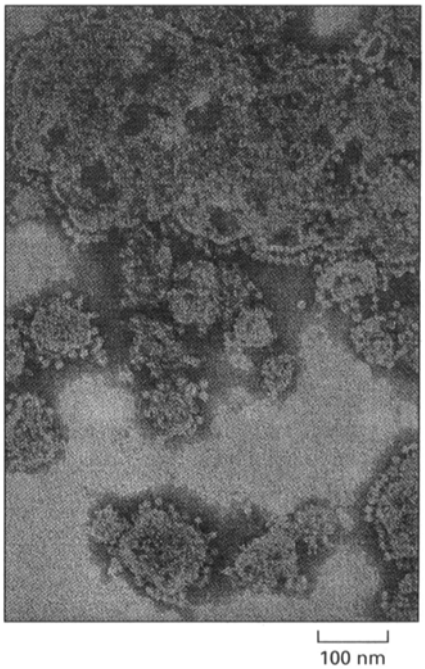
Respiratory chain (reconsidered)

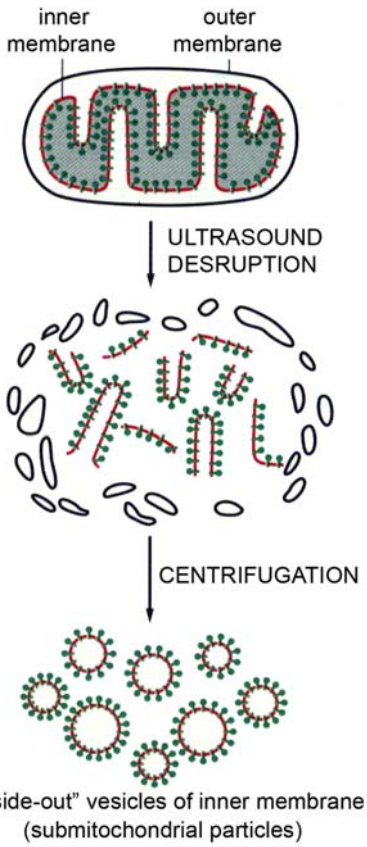
Succinate-dehydrogenase complex
- 1 flavin center; 3 iron-sulfur centers;
1 heme center (cytochrome type b)



ATP synthase (F_0F_1 ATP-ase)







- 500 kD
- Lollipop like structures (trunk, neck and head)
- At least 9 protein types (2 autonomous)
- Transmembrane domain: proton carrier
- Head and neck (3α + 3β + 1γ + + 1δ + 1ε): ATP synthase

Organization of ATP synthase

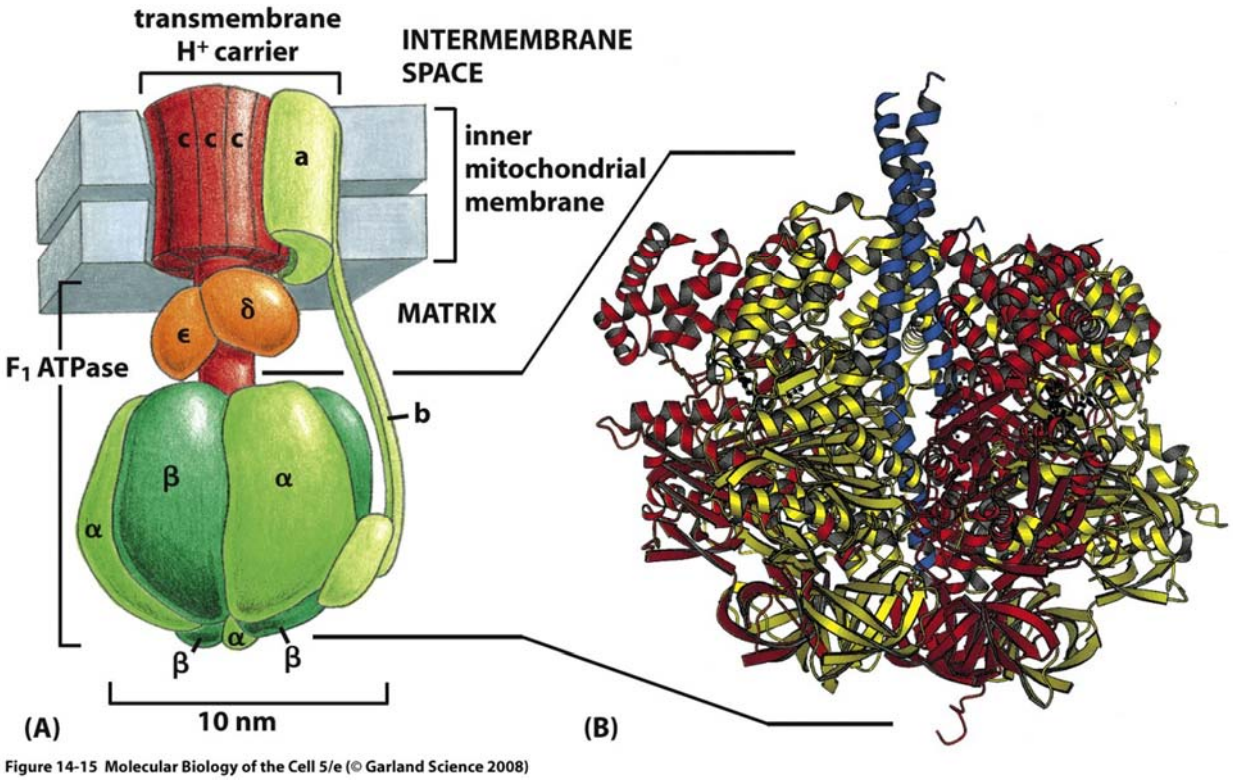
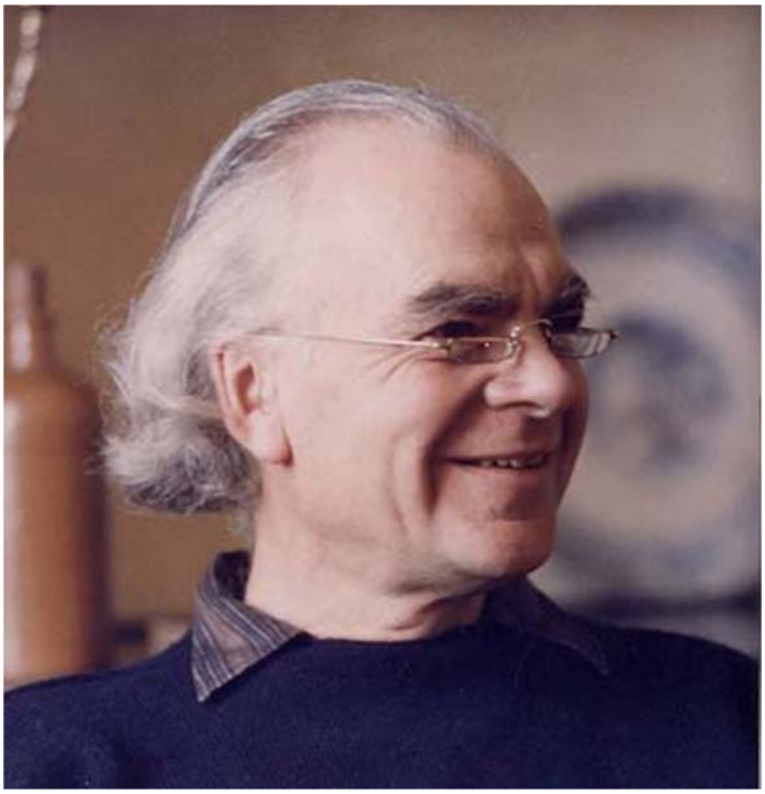


Figure 14-15 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Mitochondrion function

Chemiosmotic theory postulates (P. Mitchell, 1961)

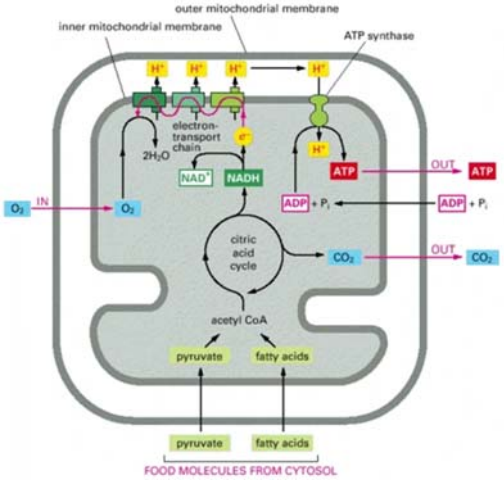
Nobel Prize winner in chemistry, 1978

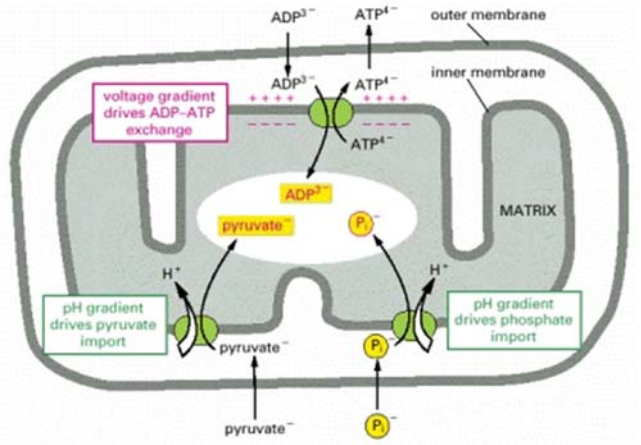


Mitochondrion function

Chemiosmotic theory postulates (P. Mitchell, 1961)

Nobel Prize winner in chemistry, 1978





1. Respiratory chain is proton translocating, pumping H^+ out of matrix and creating an electrochemical gradient at the inner membrane level;
2. ATP synthase produces ATP dissipating the proton gradient;
3. Mitochondrial inner membrane contains carrier proteins trafficking the metabolites;
4. Mitochondrial inner membrane is practically impermeable to protons and, generally speaking, to any ions;

Respiratory chain – ATP synthesis uncoupling

- Chemiosmotic coupling (coupling of respiratory chain with ATP synthase function) is essential for ATP production;
- Impeding of that results in dissipating the energy accumulated in proton gradient as heat;
- Physiological uncoupling agent, thermogenin, assure the thermal protection of the organisms.

Mitochondrion biogenesis *(i)*

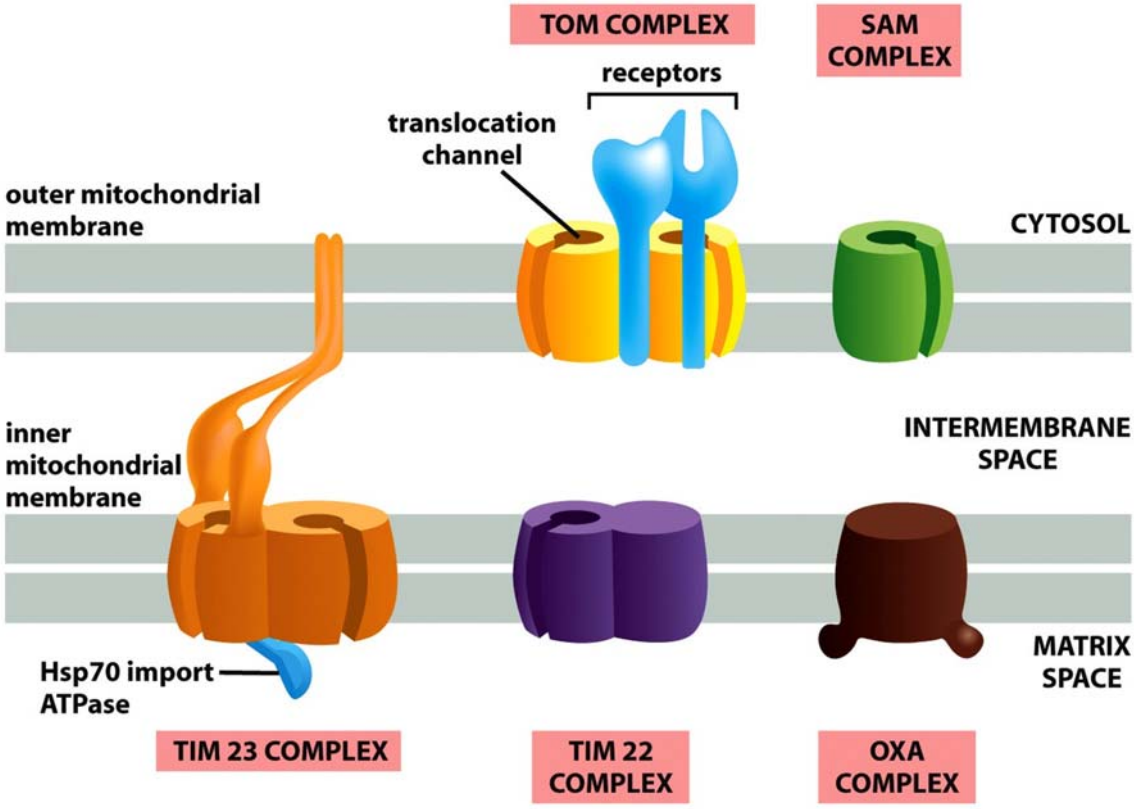
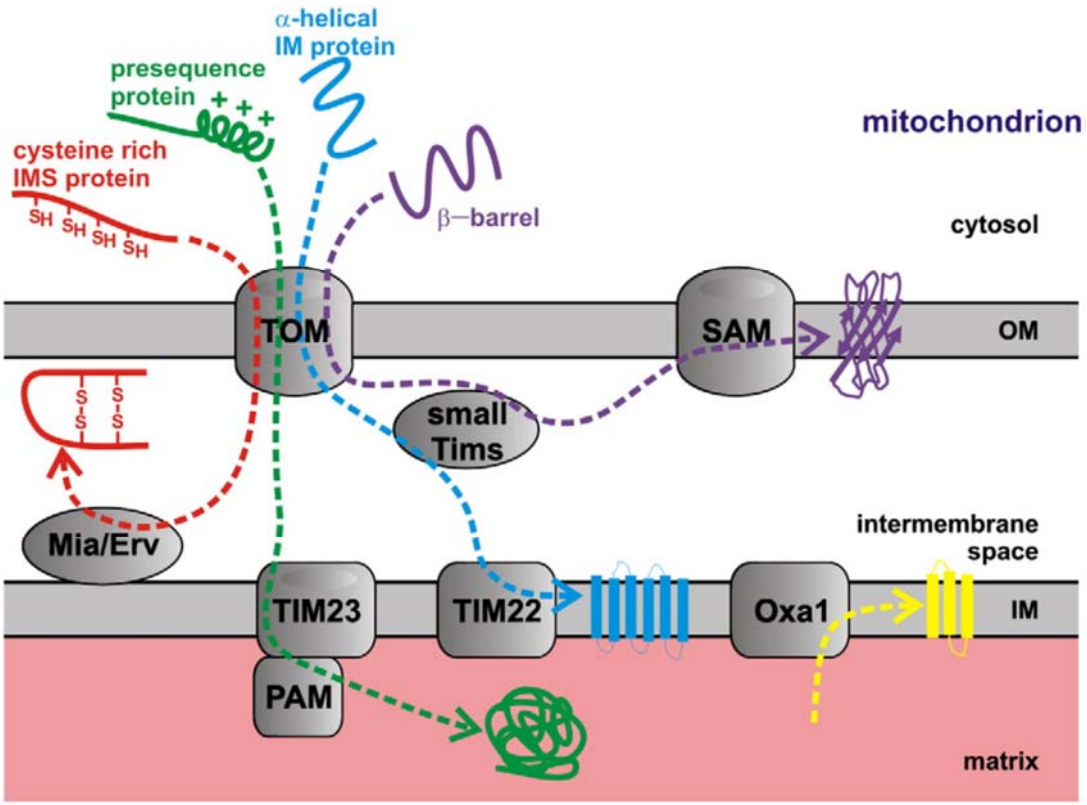


Figure 12-23 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Mitochondrion biogenesis *(ii)*



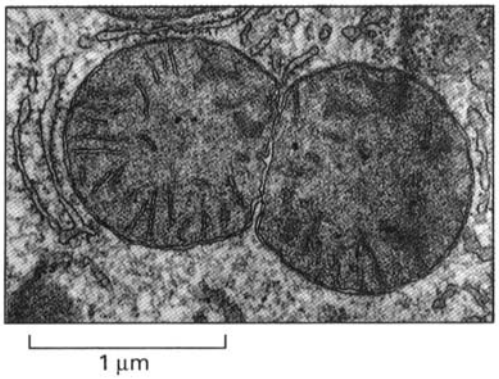
Hewitt V, Alcock F, Lithgow T. *Biochim Biophys Acta*. 2011; 1808: 947-954.

Abbreviations

- Mia – **M**itochondrial **I**ntermembrane space import and **A**ssembly
- Erv – **E**ssential for **R**espiration and **V**egetative growth (ALR – **A**ugmenter of **L**iver **R**egeneration)
- SAM – **S**orting and **A**ssembly **M**achinery
- PAM – **P**resequence translocase-**A**ssociated **M**otor
- OXA – **OX**idase **A**ssembly translocase

Mitochondrion origin

- Endosymbiotic theory;
- Arguments:
  - Cardiolipin content of inner membrane;
  - Porins in outer membrane;
  - DNA molecule in the matrix, circular (closed loop);
  - Ribosomes 70S, protein synthesis sensitive to chloramphenicol, insensitive to cycloheximide;
  - RNA polymerase sensitive to rimfamicin;
  - Independent division.



Summary

- Mitochondria are special organelles, organized by a double membrane system;
- Four ultrastructural components cooperating for the essential function: production of ATP;
- Summary of that cross-talk – chemiosmotic theory;
- Respiratory function due to the three enzymatic complexes acting in the electron transport chain, plus CoQ and cytochrome c;
- Krebs cycle provides e^- to respiratory chain using NADH and $FADH_2$;
- Proton gradient resulting in respiratory chain is dissipating for ATP production;
- Coupling ***versus*** uncoupling of respirator chain with ATP synthesis in oxidative phosphorylation is a switching mechanisms: ATP ***versus*** heat;
- Mitochondrial biogenesis does not involve a ***de novo*** production of the organelle;
- Origin of the mitochondria is due to an endosymbiotic event.