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Oxidative Phosphorylation and Electron Transport Chain

***Oxidative Phosphorylation:** A process containing formation ATP molecules during passage the electrons from NADH or $FADH_2$ to O_2 by electron transport chain (ETC), (means energy derived phosphorylation by transporting electrons from reducing powers to O_2 through respiratory chain).

***Electron Transporting:** A process includes transport pairs of electrons between coenzymes NADH or $FADH_2$ which are producing of glycolysis, β-oxidation and other pathways and have high transfer potential**.**

This process occurs in mitochondria in Eukaryotes while in plasma membrane in Prokaryotes. The electron transport chain is present in the inner mitochondrial membrane and is the final common pathway by which electrons derived from different fuels of the body flow to oxygen. Electron transport and ATP synthesis by oxidative phosphorylation proceed continuously in all tissues that contain mitochondria**.**

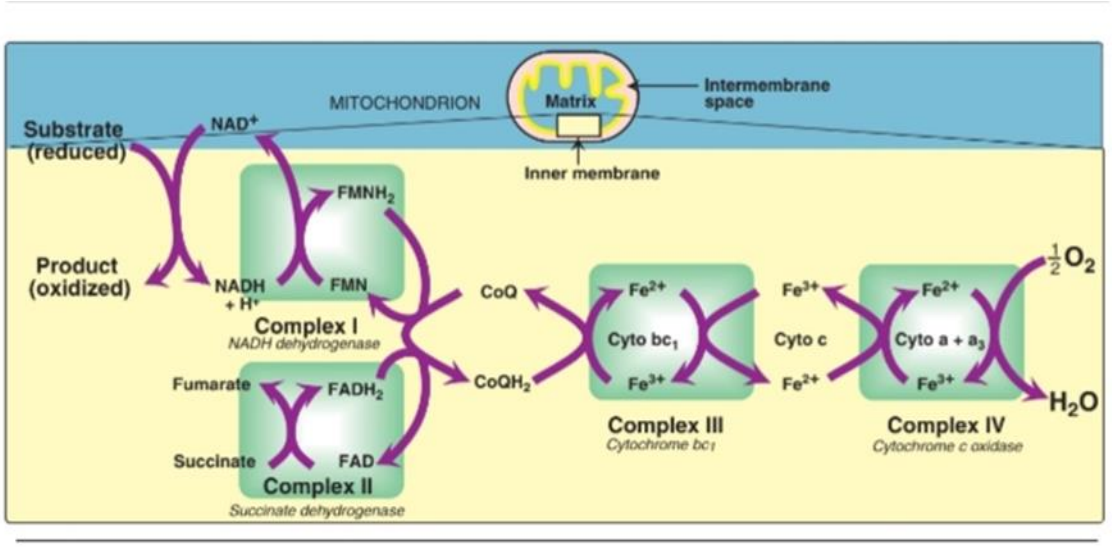
The components of the electron transport chain are located in the inner membrane. The enzymes responsible for the oxidation of pyruvate, amino acids, fatty acids (by β-oxidation), and those of the tri-carboxylic acid (TCA) cycle are found in matrix of the mitochondrion .

The inner mitochondrial membrane can be disrupted into five separate protein complexes, called Complexes I, II, III, IV, and V.Complexes I–IV each contain part of the electron transport chain. Each complex accepts or donates electrons to relatively mobile electron carriers, such as coenzyme Q and cytochrome c. Each carrier in the

electron transport chain can receive electrons from an electron donor, and can subsequently donate electrons to the next carrier in the chain. The electrons ultimately combine with oxygen and protons to form water.Complex V is a protein complex that contains a domain (Fo) that spans the inner mitochondrial membrane, and a domain (F1) that appears as a sphere that protrudes into the mitochondrial matrix .Complex V catalyzes ATP synthesis and so is referred to as ATP synthase.

***Reactions of the Electron Transport Chain**

With the exception of coenzyme Q, all members of this chain are proteins. These may function as enzymes as is the case with the dehydrogenases, may contain iron as part of an iron–sulfur center, may be coordinated with a porphyrin ring as in the cytochromes, or may contain copper as does the cytochrome a + a3 complex



1-Formation of NADH: NAD+ is reduced to NADH by dehydrogenases that remove two hydrogen atoms from their substrate. Both electrons but only one proton (that is, a hydride ion, :H–) are transferred to the NAD+, forming NADH plus a free proton, H+.

2-NADH dehydrogenase: The free proton plus the hydride ion carried by NADH are next transferred to NADH dehydrogenase, a protein complex (Complex I) embedded in the inner mitochondrial membrane. Complex I has a tightly bound molecule of flavin mono nucleotide (FMN) that accepts the two hydrogen atoms (2e– + 2H+), becoming FMNH2. NADH dehydrogenase also contains iron atoms paired with sulfur atoms to

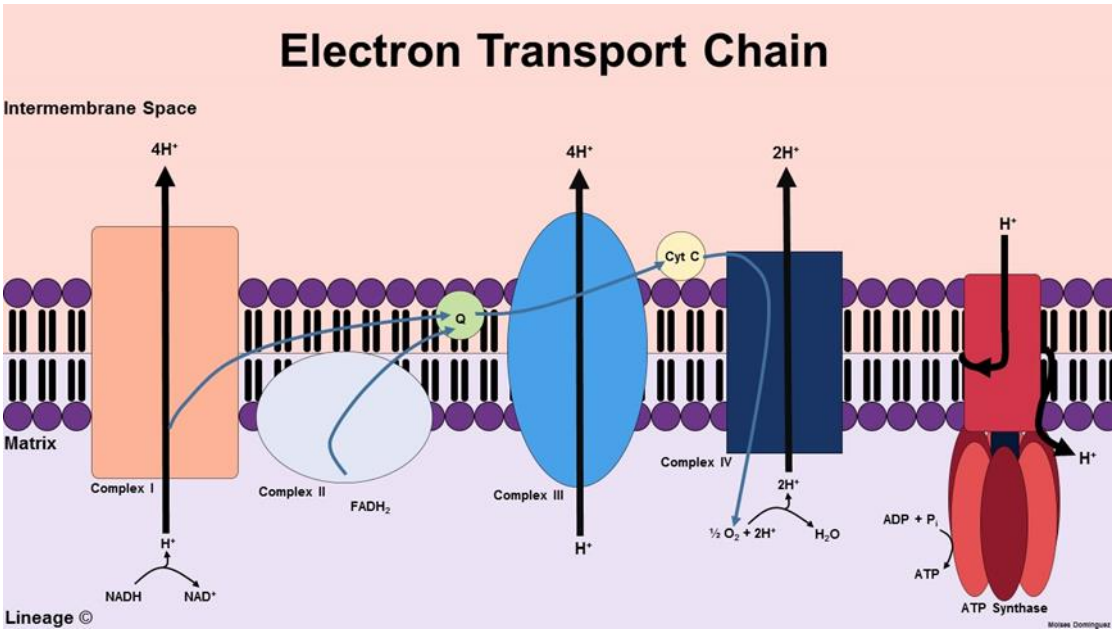
make iron–sulfur centers .These are necessary for the transfer of the hydrogen atoms to the next member of the chain, coenzyme Q (ubiquinone).

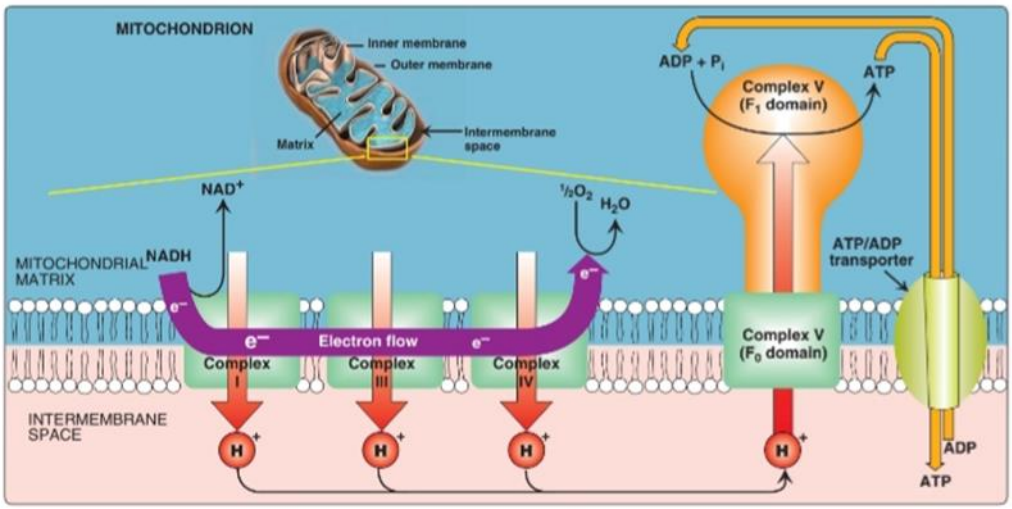
3- Coenzyme Q: Coenzyme Q (CoQ) is a quinone derivative with a long, hydrophobic isoprenoid tail. It is also called ubiquinone because it is ubiquitous in biologic systems. CoQ is a mobile carrier and can accept hydrogen atoms both from FMNH2, produced on NADH dehydrogenase (Complex I), and from FADH2, produced on succinate dehydrogenase (Complex II), glycerophosphate dehydrogenase and acyl CoA dehydrogenase. CoQ transfers electrons to Complex III. CoQ, then, links the flavoproteins to the cytochromes.

4-Cytochromes: The remaining members of the electron transport chain are cytochromes. Each contains a heme group (a porphyrin ring plus iron). Unlike the heme groups of hemoglobin, the cytochrome iron is reversibly converted from its ferric (Fe3+) to its ferrous (Fe2+) form as a normal part of its function as a reversiblecarrier of electrons. Electrons are passed along the chain from CoQ to cytochromes bc1 (Complex III), c, and a + a3 (Complex IV).

5-Cytochrome a + a3: This cytochrome complex is the only electron carrier in which the heme iron has an available coordination site that can react directly with O2, and so also is called cytochrome oxidase. At this site, the transported electrons, O2, and free protons are brought together, and O2 is reduced to water. Cytochrome oxidase contains copper atoms that are required for this complex reaction to occur.

***ATP Synthase**: The enzyme complex ATP synthase (Complex V) synthesizes ATP using the energy of the proton gradient generated by the electron transport chain. The chemiosmotic hypothesis proposes that after protons have been pumped to the cytosolic side of the inner mitochondrial membrane, they reenter the matrix by passing through a channel in the membrane-spanning domain of Complex V, driving rotation of Fo and, at the same time, dissipating the pH and electrical gradients. Fo rotation causes conformational changes in the extra-membranous F1 domain that allow it to bind ADP + Pi, phosphorylate ADP to ATP, and release ATP.





***Hypotheses of Oxidative Phosphorylation**

There are 3 hypotheses interpret oxidative phosphorylation:

1-Chemical Coupling Hypothesis: is presented by (Slater) and depends on formation intermediate compound rich in energy used to form ATP during transfer of electron from reducing powers to O_2 .

2-**Change in the Protein's Three-Dimensional Structure Hypothesis**: is presented by (Boyer) and states on transfer electrons from reducing powers to O_2 , leads to change

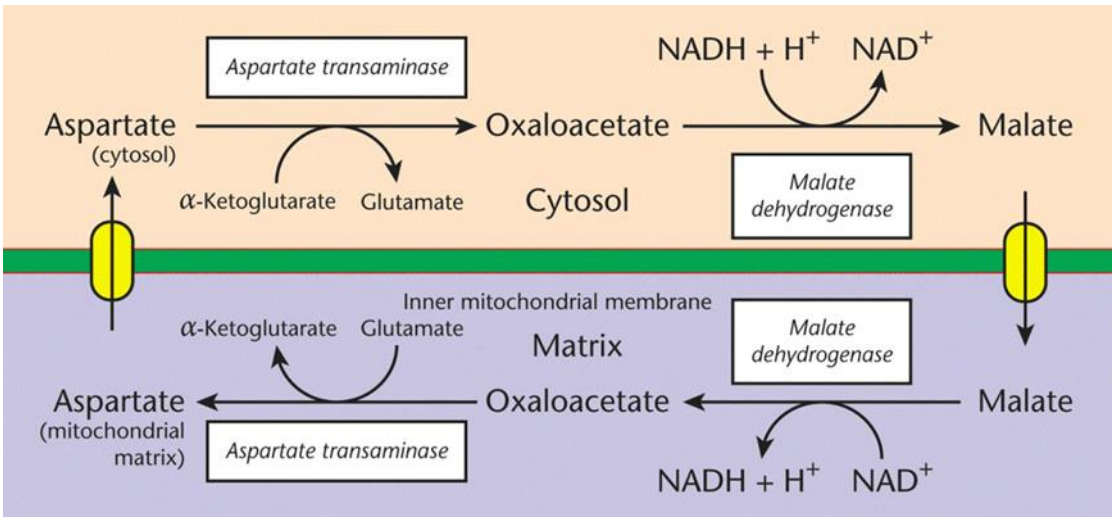
protein's three-dimensional structure in respiratory chain and then formation energy as ATP.

3-Chemiosomotic Hypothesis: is presented by (Mitchell) and considered that mitochondrial inner membrane is impermeable of protons (H^+) through transfer electrons from NADH or $FADH_2$ to O_2 and that will lead to transfer (H^+) to mitochondrial inter membrane space. In this case, protons (H^+) are the motive force to formation ATP by ATP synthase.

***How NADH Component Outside Mitochondria Enters the Respiratory Chain and Oxidative Phosphorylation?**

NADH or $FADH_2$ formed by Crib's cycle enter to oxidative phosphorylation directly, because it occurs inside of mitochondria. But NADH formed outside of mitochondria by glycolysis will not be useful unless enter to mitochondria, so there are two ways to entrance:

1-Malate – Aspartate Shuttle: This way includes transfer (ē) from NADH to oxaloacetate that is reduced by malate dehydrogenase to malate which enters to mitochondria and oxidized by malate dehydrogenase to oxaloacetate, so electrons will be released as NADH and enter to oxidative phosphorylation. After that oxaloacetate will be converted to aspartate which in turn goes out to cytoplasm to repeat the cycle again. In this shuttle, oxidation of NADH will produce 3 ATP. This occurs in heart, kidney and liver.



2-Glycerol Phosphate Shuttle : This way includes transfer (ē) from NADH to dihydroxyacetone phosphate which is reduced by glycerol3-phosphate dehydrogenase to glycerol3-phosphate and enters to mitochondria then converted to dihydroxyacetone by FAD. In this way $FADH_2$ enters to oxidative phosphorylation and gives 2 ATP. This occurs in muscles and brain.

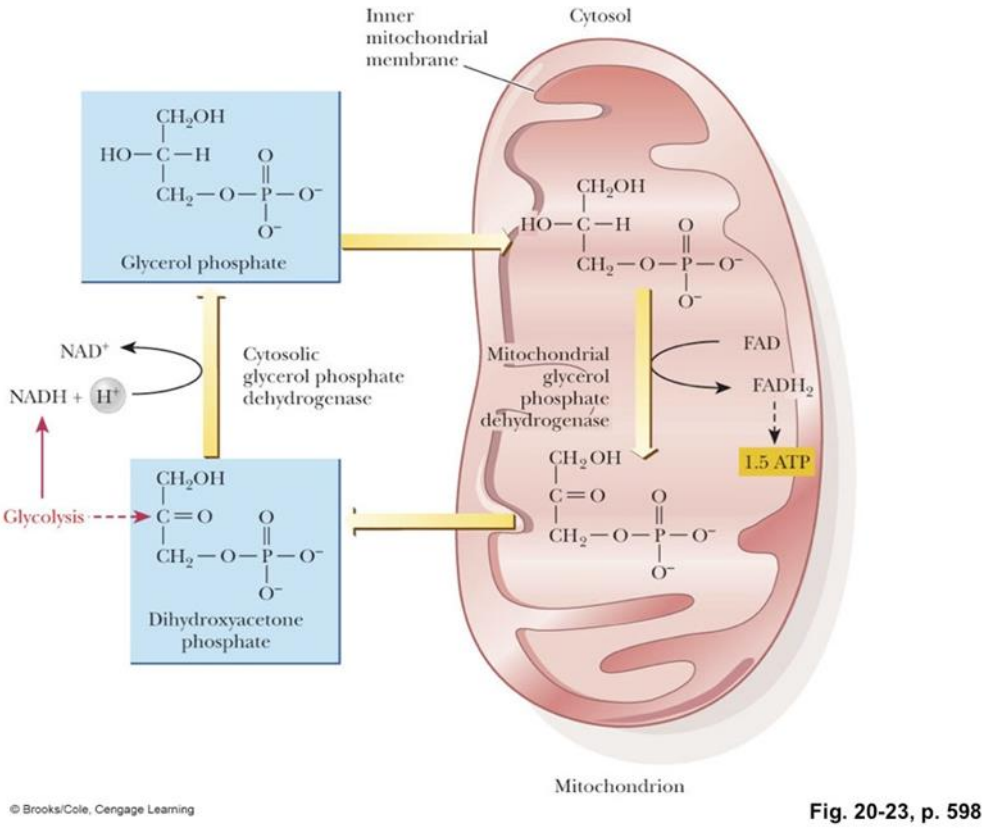


Fig. 20-23, p. 598

***Types of Phosphorylation: There are 2 types of phosphorylation**:

1-Substrate Level Phosphorylation: It occurs in case of converting 1,3 diphosphoglycerate to 3-phosphoglycerate or phosphoenol pyruvate to pyruvate. Both of them occur in cytoplasm (where ATP producing by binding ADP with Pi) and mitochondria (by phosphorylation of GDP to GTP in Cribs cycle).

2-Oxidative Phosphorylation: It includes formation of ATP by binding ADP with Pi and produce high energy through transfer electrons from NADH or $FADH_2$ to O_2 .

***Inhibitors of Oxidative Phosphorylation and Electron Transport Chain:**

There are some substances inhibits binding ADP with Pi to formation ATP such as valinomycin and gramycin which increase the entrance of (H^+) to mitochondrial inner membrane and that leads to decrease motive force forming to ATP. Also presence of cyanide, carbon oxide (CO) and Rotenone leads to inhibition transfer electrons through respiratory chain.

Reference:

1. Harvey,R. and Femier, D. (2012).Lippincott's Illustrated Reviews Biochemistry.6th ed. Willam and Wilkins.