Biological Oxidation

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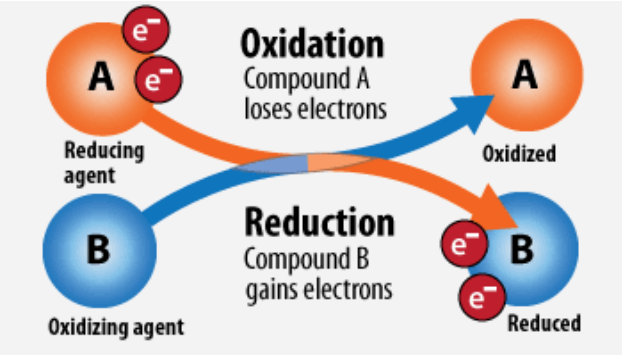
Learning Objectives

- Know what is cellular respiration? where does it happen?
- Understand Electron Transport chain components
- Define oxidative phosphorylation
- Clinical Importance of different compositions of the chain

Cellular Respiration:

is a process by which cell derive energy in the form of **ATP** from controlled reaction of hydrogen with oxygen to form water.

Oxidation Vs Reduction



What is ATP

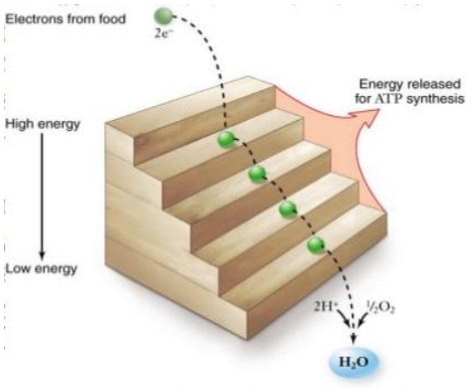
The adenosine triphosphate (ATP) molecule is essential for life.
It provides energy for muscle contraction, nerve conduction, biochemical reactions

How this ATP formed??

- Production of ATP by substrate-level phosphorylation
- Production of ATP from phosphocreatine
- Production of ATP from ADP by adenylate kinase (myokinase)

Oxidative phosphorylation

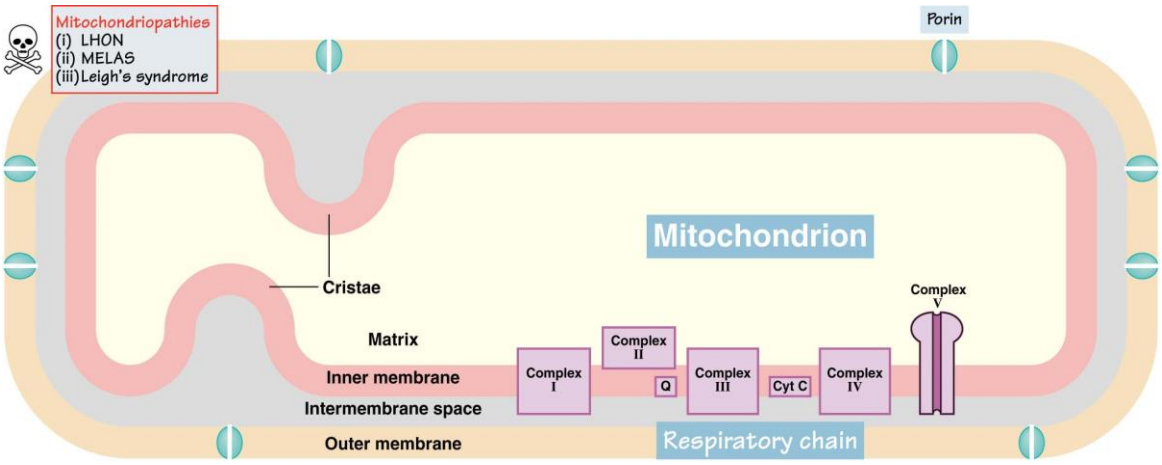
is a series of reactions which **couples** the oxidation of reduced coenzymes to the phosphorylation of ADP and generation of ATP



- the electron passed down the electron transport chain,
- free energy lost,
- Lost energy captured and stored by production of ATP from ADP and inorganic phosphate.
- The energy not trapped will release as heat

Electron Transport Chain

Respiratory chain mainly take place inside in the mitochondrion, which have been termed the "**powerhouses**" of the cell.



Outer membrane:

freely <u>permeable</u> to most of ions and small molecules

presence of various enzymes

Acetyl CoA synthase

Glycerol phosphate acyltransferase

Inner membrane

is *<u>impermeable</u>* to most small ions, including H^+, Na^+, K^+, and small molecules such as **ATP**, **ADP**, Pyruvate and other.

rich in protein, half of which is directly involved in electron transport and oxidative phosphorylation

highly convoluted and convolutions called **cristae**

ATP Synthase complexes attach to the inner surface which also referred to inner membrane particles

Matrix

this gel – like solution in the interior of mitochondria

50% protein.

enzyme responsible for oxidation of pyruvate, amino acid and fatty acid and TCA Cycle, oxidized form of coenzyme, mitochondrial RNA and DNA (mRNA and mDNA)

Why DNA present in the mitochondria in addition to the nucleus??

Organization of Chain

The inner mitochondrial membrane can be disrupted into five separate enzyme complexes I, II,III,IV, V

The four complex I – IV are embedded in the inner mitochondrial membrane

The **CoQ** and **cytochrome C** are mobile

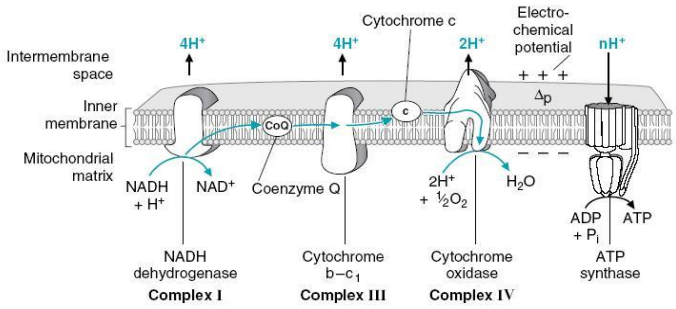
Complexes from I – IV constitute the electron transport chain

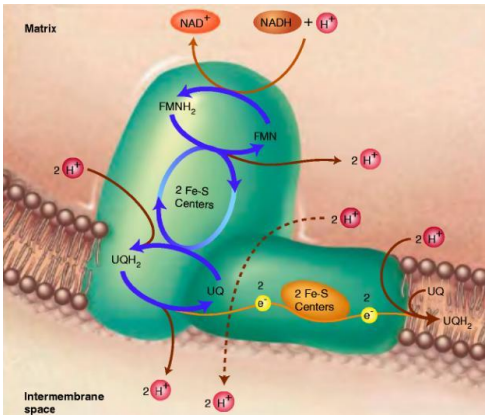
Complex I NADH Dehydrogenase

Complex II Succinate Dehydrogenase

Complex III Cytochrome bc Complex

Complex IV Cytochrome Oxidase





Complex I NADH Dehydrogenase

complex that contains a binding site for

- NADH,
- FMN
- Fe-S center binding proteins
- CoQ .

Coenzyme Q (Ubiquinone)

CoQ not protein bound.

CoQ hydrophobic which enables it to freely diffuse among the lipids of the inner mitochondrial membrane.

When the oxidized quinone form accepts a single electron (to form the semiquinone),

Complex II Succinate Dehydrogenase

part of TCA in the inner mitochondrial membrane

mediate the transfer of electron from succinate to UQ.

succinate dehydrogenase enzyme iron – sulfur proteins.

This molecule also contains covalently link FAD.

Complex III

Complex IV

Question

How can NADH produce in the cytoplasm oxidize in the cellular respiration?

The Chemiosmotic Theory

As the electron pass through the electron transport chain, protons are transported from the matrix and released into the intermembrane space. As a result, an electrical potential and proton gradient arise across the inner membrane. This proton gradient is referred to as the ***Protonmotive force***

ATP synthase

Multi- subunit enzyme consists of inner membrane portion, in addition to Stalk and head piece that project into the matrix. The transfer of protons through the channel in ATP synthase complex result in synthesis of ATP from ADP + Pi and at the same time dissipating the pH and electrical gradient

The control of oxidative phosphorylation

- Availability of ADP
- Inorganic phosphate
- ADP/ATP transporter

Energy Yield from Electron transport chain

4 Protons	Complex I
4 Protons	Complex III
2 Protons	Complex IV

With ***3 protons*** translocated for each **ATP Synthesis**

3 ATP for each NADH oxidized
2 ATP for each FADH oxidized

Respiratory Chain inhibition

- *Inhibitory of electron transport system*
- *Inhibitory of oxidative phosphorylation*
- *Uncoupler of oxidative phosphorylation*

Inhibitory of Electron transport system

These compounds prevent the passage of electron by binding to the component of the chain blocking the oxidation/ reduction of reaction

In anoxia: the absence of O2 there is no ATP generated from oxidative phosphorylation because the electron back up in the system

- **Barbiturate** (amobarbital) inhibit electron transport via complex I by blocking the transfer of electron from Fe-S to CoQ.
- **Malonate**: compensatory inhibitor of complex II
- **Antimycin A and Dimercaprol**: inhibit complex III
- **Cyanide, Carbon monoxide, H_2S**: inhibit Complex IV and therefore totally arrest respiration by binding to Fe in Heme of cytochrome

Inhibitor of oxidative phosphorylation

Oligomycin:

drug bind to Stalk of ATP synthase closing the H channel prevent the re entry of proton into the inner mitochondrial matrix

How can plant toxin **Atractyloside**
interfere with oxidative phosphorylation ???

Uncoupler

Def:

compound that dissociate the oxidation in the respiratory chain from phosphorylation causing respiration to become uncontrolled. In this phenomenon, proton leak back into the matrix without going through ATP synthase Pore. Dissipate the electrochemical gradient across the membrane without generating ATP

Chemical (Synthetic) Uncoupler

<u>2,4 Dinitophenol</u> is the classical uncoupler. It is lipophilic proton carrier that readily dissolve through mitochondrial membrane

Physiological uncoupler

This is occurred by uncoupling protein that form proton conductance channel through the membrane
These protein create proton leak that allow proton to reenter the mitochondrial matrix without energy being captured as ATP (Energy release as Heat)
This protein is called **Thermogenin**
Thermogenin is responsible for activation of fatty acid oxidation and heat production in the Brown Adipose Tissue

This thermogenin protein found in the inner mitochondrial membrane that had channel through which proton pass back to the matrix
Under normal condition these channels is plugged by GDP so remain closed
When the brown fat stimulated by cold exposure GDP plug will be lost and proton pass back into the matrix and energy will release as heat
So, in this case brown fat maintaining a constant internal environment. And involve in the temperature regulation