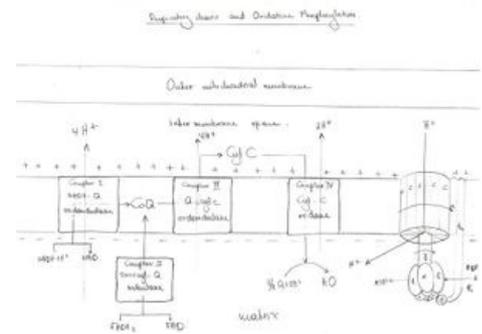


# Respiratory chain Oxidative phosphorylation

## Respiratory chain and Oxidative phosphorylation

### Respiratory chain

The respiratory chain is a collection of enzymes that induce the electrochemical gradient of protons ( $H^+$ ), necessary for the ATP synthesis. Fatty acid, amino acid and monosaccharide metabolism yields acetyl-CoA, a molecule that is oxidized in the Citric acid cycle producing reduced coenzymes ( $NADH+H^+$ ,  $FADH_2$ ) and GTP. These coenzymes are subsequently collected and transported by the respiratory chain, directing them to their final reaction with  $O_2$  to form  $H_2O$ . The respiratory chain consists of enzymes that are found only in the inner membrane of mitochondria, thus only mitochondrion-containing cells are able to produce energy through oxidative phosphorylation (aerobic respiration). Mitochondrionless cells, such as erythrocytes, produce energy only through glycolysis, an anaerobic process of glucose oxidation into pyruvate.



### Oxidative phosphorylation

It is the process through which the liberated free energy provided by the electrochemical gradient of protons ( $H^+$ ), is trapped as high energy phosphate. The electrochemical built-up of hydrogen ions, by the respiratory chain is used to drive protons through an enzyme called ATP synthase. The kinetic energy of protons is used by the synthase to store energy as high energy phosphate in ATP by binding ADP and  $P_i$ .

## Components of the respiratory chain

Electrons flow through the respiratory chain, passing through three large protein enzyme complexes.

1. **NADH-Q oxidoreductase/Complex I:** the electrons are transported from the  $NADH+H^+$  to coenzyme Q
2. **Q-Cytochrome c oxidoreductase/Complex III:** coenzyme Q passes the electrons to the cytochrome c
3. **Cytochrome c oxidase/Complex IV:** completes the chain, passing the electrons to  $O_2$  and causing it to be reduced to  $H_2O$
4. **Succinate-Q reductase/Complex II:** the electrons are transferred from  $FADH_2$  to coenzyme Q

The flow of electrons through the respiratory chain generates ATP through the process of oxidative phosphorylation. Enzyme complexes I, III and IV act as proton pumps which cause the accumulation of protons in the intermembrane space of mitochondria constituting it more positive than the intramembrane space (matrix) which becomes progressively more negative building an electrochemical gradient with protons having the tendency to return back into the matrix which is more negative. The only way to do that is passing through the ATP synthase which exploits their energy to form ATP.

## Inhibitors

### Inhibitors of the respiratory chain:

- Barbiturates: they inhibit complex I/NADH-Q oxidoreductase, preventing electron transfer from  $NADH+H^+$  to coenzyme Q
- $CO_2$ ,  $H_2S$  and  $CN^-$ : they inhibit complex IV/cytochrome c oxidase preventing reduction of  $O_2$  to  $H_2O$
- Antimycin A: it inhibits complex III/Q-cytochrome c oxidoreductase preventing transfer of electrons from CoQ to cyt c.

**Inhibitors of the oxidative phosphorylation:** atractyloside which inhibits ATP synthase by blocking the flow of protons through the  $F_0$  subunit. **Uncouplers of oxidative phosphorylation:** 2,4 dinitrophenol which uncouples proton pumping from ATP synthesis because it carries protons across the inner mitochondrial membrane (no ATP synthase inhibition, rather elimination of the proton electrochemical gradient built-up)

## Links

## Bibliography

MURRAY, Robert K. - BENDER, David A.. *Harper's Illustrated Biochemistry*. 29<sup>th</sup> edition. McGraw-Hill Companies, Inc., 2012. ISBN 978-0-07-176576-3.

