SIXTH CHAPTER: Bioenergetic

Living organisms are highly complicated at the molecular level. A large amount of energy is invested in maintaining the ordered and complicated state of cells and tissues. In humans and animals, energy needed for work and biosynthesis of cellular structures is derived from organic molecules in the diet. Often these come from plant sources, who derived their energy for synthesis of biomolecules from sunlight. In animals, energy is derived from the breakdown of fuel molecules by processes referred to as catabolism. In turn, the energy released from catabolism is used to drive biosynthetic processes collectively referred to as anabolism.

Bioenergetics is the science which studies the set of energetic reactions at the level of the cells of the living organism.

I. Types of chemical reaction

Nutrients are organic or mineral molecules that do not need to be transformed to be absorbed and used by a cell. Organic nutrients come from food after the action of digestive enzymes.

Metabolites are molecules transformed by enzymatic reactions to produce energy or other chemical compounds.

Metabolism is the set of chemical reactions of transformation of matter and energy which take place in all living cells. Metabolism brings together two types of reactions:

- Material degradation reactions (catabolism) which produce energy: exergonic reactions (nutrient degradation reactions) or exothermic;

  Example : $$C_6H_{12}O_6 + 6\,O_2 \underset{2}{\overset{1}{\rightleftharpoons}} 6\,CO_2 + 6\,H_2O + \text{Energie}$$

- Synthesis reactions of matter (anabolism) which consume energy: endergonic reactions (biogenesis, muscle contraction, nerve impulses, etc.) or endothermic.

Example: Starch and glycogen are storage forms of glucose in living plant and animal cells respectively.

Generally, the main metabolites used by the cell are: glucose, fatty acids, triglycerides (lipids) and amino acids.

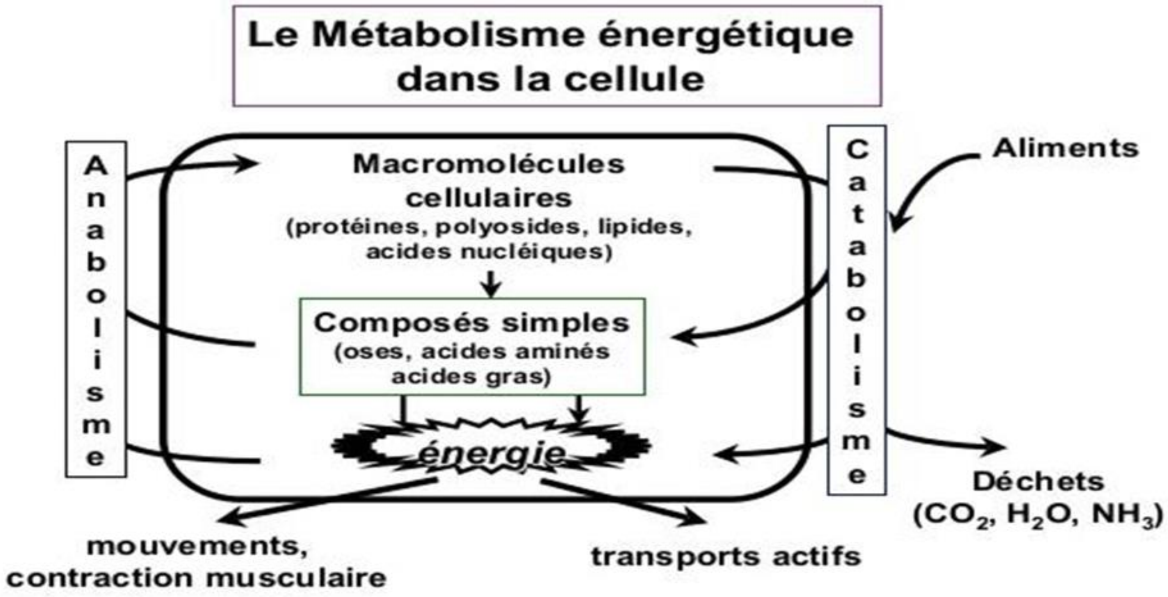

Fig 1. Molecular renewal.

II. Oxidative Energy

The primary mechanism used by non-photosynthetic organisms to obtain energy is oxidation.

Oxidation/reduction

Chemical energy can be stored in the form of electrons with high energy potential contained in energy molecules.

Oxidation is a chemical reaction during which a molecule (a reducing agent) loses one or more electrons or hydrogen(s). A reduction is a chemical reaction during which a molecule (an oxidant) captures one or more electrons or hydrogen(s).

For every biological oxidation, there is a corresponding reduction - one molecule loses electrons to another molecule. Oxidation reactions tend to release energy and are a source of bioenergy.

Acétate + $2H^+ + 2e^-$ $\longleftrightarrow$ Acétaldéhyde

$NAD^+ + 2H^+ + 2e^-$ $\longleftrightarrow$ $NADH,H^+$

Pyruvate + $2H^+ + 2e^-$ $\longleftrightarrow$ Lactate

$$\frac{1}{2} O_2 + 2H^+ + 2e^- \longleftrightarrow H_2O$$

Catabolic processes are often oxidative in nature and energy releasing. Some, but not all of that energy is captured as ATP. If not all of the energy is captured as ATP, what happens to the rest of it? The answer is simple. It is released as heat and it is for this reason that we get hot when we exercise. By contrast, anabolic processes are often reductive in nature and require energy input.

Energy Coupling

Cells overcome the energy obstacle by using ATP. Hydrolysis of ATP provides energy for the enzyme to stimulate the reaction on the other substance(s)

There are, other reasons that organisms need energy. Muscular contraction, synthesis of molecules, neurotransmission, signaling, thermoregulation, and subcellular movements are examples. Where does this energy come from? The currencies of energy are generally high-energy phosphate-containing molecules. ATP is the best known and most abundant, but GTP is also an important energy source (required for protein synthesis). CTP is involved in synthesis of glycerophospholipids and UTP is used for synthesis of glycogen. In each of these cases, the energy is in the form of potential chemical energy stored in the multi-phosphate bonds. Hydrolyzing those bonds releases the energy in them.

Cellular Phosphorylations

Formation of triphosphates is essential to meet the cell's immediate energy needs for synthesis, motion, and signalling.

Of the triphosphates, ATP is the primary energy source, acting to facilitate the synthesis of the others. ATP is made by three distinct types of phosphorylation – oxidative phosphorylation (in mitochondria), photophosphorylation (in chloroplasts of plants), and substrate level phosphorylation (in enzymatically catalyzed reactions).

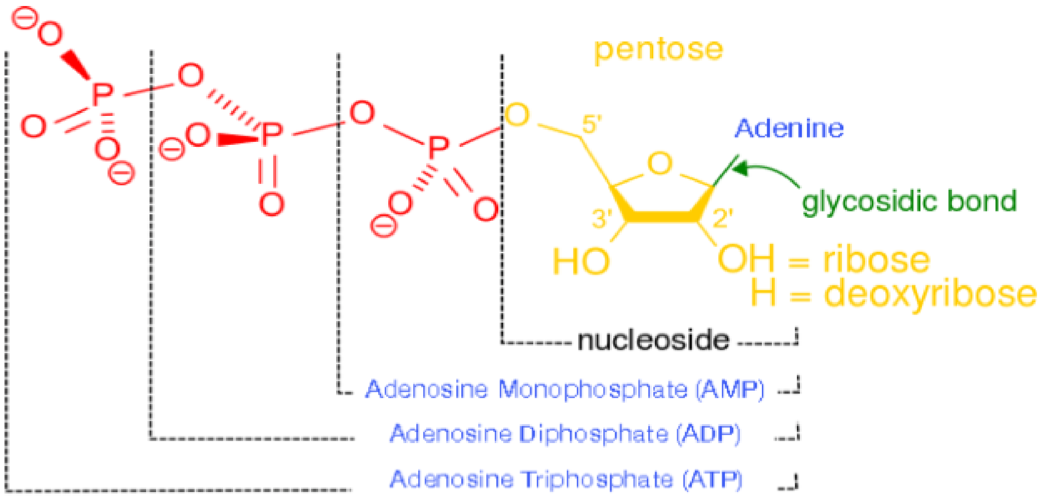

Fig 2. ATP.

The respiratory chain and oxidative phosphorylation

Much of the energy produced in the carbohydrate, lipid and protein catabolic pathways is found contained in NADH and $FADH_2$, it must be converted into ATP (rapidly usable energy) which is produced in the mitochondria from the mitochondrial respiratory chain and oxidative phosphorylation: reduced mitochondrial coenzymes (NADH and FADH2) give up (lose) their two electrons to a system of transporters which, through a cascade of redox reactions, brings these electrons to the final acceptor, molecular oxygen.

However, during this electronic transfer, a proton gradient is formed on either side of this membrane, which allows the synthesis of ATP during a reaction catalyzed by mitochondrial ATP synthetase. Respiration and ADP phosphorylation are therefore coupled via this proton gradient.

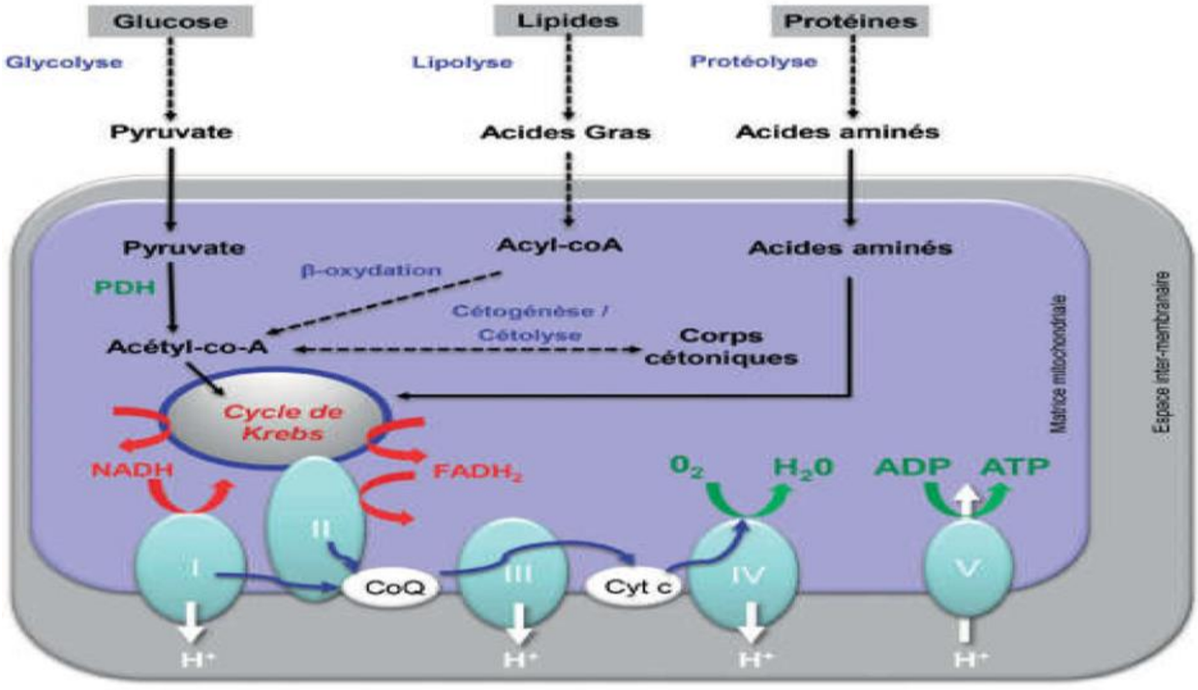

Fig 3. Mitochondrial energy metabolism.

The respiratory chain is an electron transport chain carrying out the oxidation (loses one or more electrons or hydrogen) of reduced coenzymes resulting from the degradation of organic or mineral compounds. This electron transport chain is made up of four protein complexes.

Electron Transport

Throughout the respiratory chain, electrons coming from NADH and FADH2 will lose energy which will be used to form the electrochemical proton gradient between the inter-membrane space and the mitochondrial matrix. The energy-rich electrons thus recovered will be transported successively via the different complexes:

- **Complex I** has a NADH coenzyme Q reductase action, recovering electrons from NADH and allowing the transport of protons from the mitochondrial matrix to the inter-membrane space.
- **Complex II** has a Succinate coenzyme Q reductase action, recovering electrons from FADH2 and allowing the transport of no protons.
- **Complex III** has a Coenzyme Q cytochrome C reductase action, and allows the transport of protons from the mitochondrial matrix to the inter-membrane space.
- **Complex IV** has a Cytochrome C oxidase action, and allows the transport of protons from the mitochondrial matrix to the inter-membrane space.

Coenzyme Q (or ubiquinone) and cytochrome C are electron transport molecules of the respiratory chain. Coenzyme Q allows the transition between complex I or II and complex III. It is interesting to note that coenzyme Q also accepts electrons from the cytosol. Cytochrome C allows the transition between complex III and complex IV.

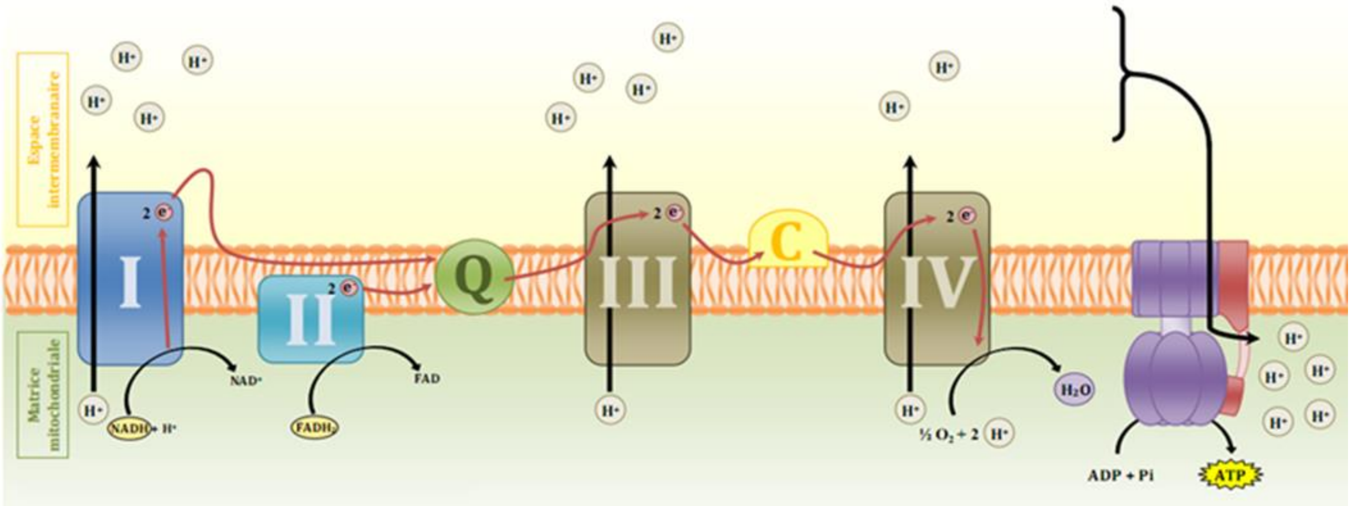

Fig 4. Simplified diagram representing the mechanisms of the respiratory chain and ATP synthesis by oxidative phosphorylation.

The electrons released at the end of the respiratory chain will react with the oxygen molecules and protons present in the mitochondrial matrix to form water molecules.

ATP Synthase

The accumulation of positive charge in the outer surface of the membrane and negative charge in the matrix generates an electrochemical gradient. This electrochemical gradient is in itself a very significant energy potential which will be used to operate the ATP synthetase pump.

The return of protons into the matrix occurs at the level of specific passages constituted by ATP synthetase (an ion pump constitutes FoF1 complexes): Fo is a transmembrane channel which selectively lets protons pass, F1 contains the catalytic site responsible for the synthesis of ATP from ADP and Pi. The electrochemical gradient of protons thus provides the energy necessary for the synthesis of ATP. (ATP synthesis is coupled to the transfer of electrons by the proton gradient: oxidative phosphorylation).

The ATP Synthase itself is an amazing nanomachine that makes ATP using a gradient of protons flowing through it from the intermembrane space back into the matrix. The movement of protons through the ATP Synthase causes it to spin like a turbine, and the spinning is necessary for making ATP.

The passage of protons through this pump activates it to form ATP from ADP + Pi.

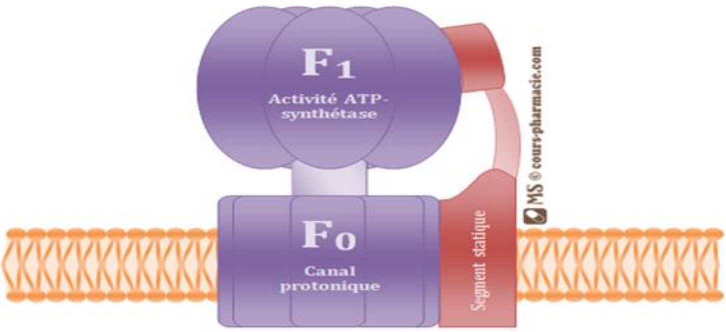

Fig 5. ATP synthase (Complex V).

Assessment of the respiratory chain:

10 NADH2 → 10 NAD + 10 H2

2 FADH2 → 2 FAD + 2 H2

6 O2 + 12 H2 → 12 H2O

34 ADP + 34 Pi → 34 ATP

10 NADH2 + 2 FADH2 + 6 O2 + 34 ADP + 34 Pi → 10 NAD + 2 FAD + 12 H2O + 34 ATP.