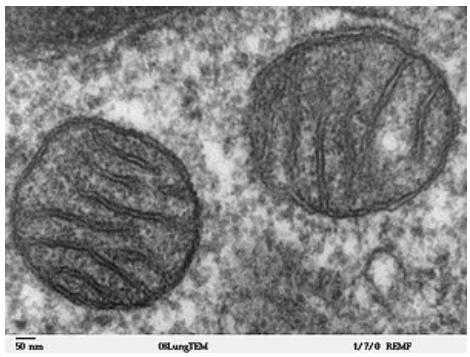
# Mitochondria

## Basic information

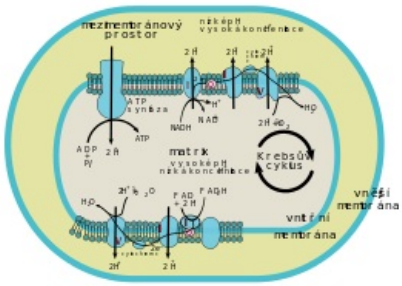
Mitochondria are membrane-bound cell organelles found in eukaryotic cells. Their basic function is the production of energy for the organism.



Mitochondria in an electron microscope

**Mitochondria** probably evolved from free-living bacteria that entered other cells, which is why they have a **double membrane**. Over time, parts of their genome moved into the nucleus of the "host" cell, making them dependent on it and unable to live independently. However, their **proteosynthetic apparatus** has been preserved, with all the features of **prokaryotes** (e.g. 70 S ribosomes). New mitochondria are created by division of existing ones ( *elongation* ). We speak of them as **semi-autonomous** (semi-independent) organelles. Plant **plastids** had a similar fate.

Mitochondria have become an integral part of all eukaryotic cells (except erythrocytes and keratinocytes). The number of mitochondria in a cell depends on its *energy needs*, it can reach up to 2000. They are especially numerous in cells with high energy demands, where they ensure the supply of energy to the processes taking place in them (e.g. muscle contraction, ion pump, activity , transport through epithelia, secretory activity liver cells). Mitochondria are either scattered in the cell or **clustered at places with high energy consumption** (e.g. basal body, kinocilia, active membrane transport in renal tubules). In living cells, they move in slow oscillatory or circular movements, which is accompanied by changes in their size.



What happens on the membranes of mitochondria.

## Types of mitochondria

### Mitochondria with cristae

They are the most common type of mitochondria in the human body, their cristae extend as membrane plates or ridge compartments from the inner mitochondrial membrane. The cristae are usually arranged perpendicular to the long axis of the mitochondria.

### Tubular-type mitochondria

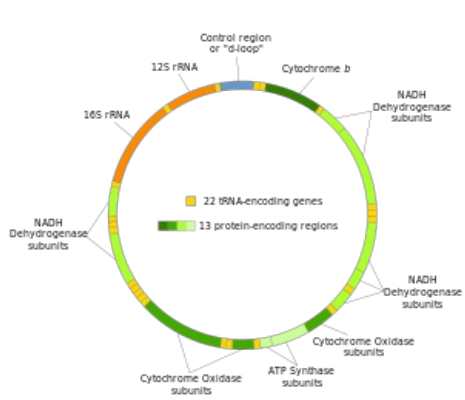
They contain tubular differentiations of the inner membrane. In humans, they occur in cells involved in the synthesis of **steroid hormones** (e.g., adrenal cortex cells , interstitial Leydig cells in the seminiferous tubules of the testes, thecal cells in ovarian follicles, and placental cells).

### Saccular-type mitochondria

In the mitochondria of the saccular (sometimes vesicular) type there are tiny vesicles that are connected to the inner mitochondrial membrane by means of short stalks. They occur in the cells of the adrenal cortex.

### Prismatic-type mitochondria

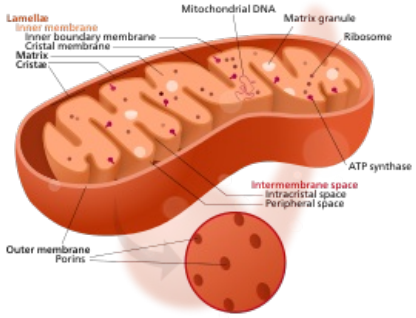
The presence of longitudinal structures with a triangular or rhomboid outline in cross-section is typical for them. They have been described in the glial cells of the central nervous system of some animals.



Mitochondrial DNA.

## Mitochondrial structure

The length of mitochondria ranges from **0,5 to 10 µm**[1] and their thickness from 0.3 to 0.5 µm. The shape, size and their number depend not only on the type of cells, but also on the metabolic activity, or on the pathological condition. They can branch and then form cylindrical structures that can be connected to each other to form a **mitochondrial network**, spread throughout the cell.



Mitochondrial membranes

# Membrane

Mitochondria are enveloped **by two full-fledged membranes**, the composition of which differs significantly.

## Outer membrane

The outer membrane has similar properties to other membrane organelles. Its shape resembles a simple ovoid or tube, it is not wrinkled. About 40% of the total weight is lipids. There is little cardiolipin. in it . It is very permeable – especially to ions. It contains translocator integral membrane proteins called **porins**. They are actually channel proteins permeable to molecules < 5 kDa.

## Inner membrane

The inner mitochondrial membrane is **wrinkled**, either in the form of simple protrusions (*cristae*),or tubes that pass through the mitochondrial cytoplasm (*tubular mitochondria*). *The crystalline type of* mitochondria is represented most often in the cells of the human organism, while the tubular type of mitochondria is found mainly in endocrine cells that produce steroid hormones. Wrinkling increases the surface area of the membrane **several times.** The number of tubules and cristae corresponds to ATP consumption. The total weight of lipids here is only 20%, proteins predominate, represented by 80%. The rest is made up of transport proteins and proteins respiratory chain. The inner membrane is selectively permeable due to the presence of transporters and pumps. It is rich in proteins, the majority of which are multienzyme complexes of the respiratory chain and ATP synthase. It is poorly permeable to ions. This characteristic is due to the high content of the phospholipid cardiolipin in the lipid bilayer.

On the side facing the matrix, the inner membrane has numerous **elementary bodies**, also called **ATP-osomes** (adenosine triphosphatosomes, oxisomes). Each body corresponds to one protein complex on which ATP synthesis takes place. They are spherical formations with a diameter of around **85 nm**, which are connected by a thin stalk to the membrane from which these particles emerge.

The inner membrane and elementary bodies are thought to be the sites where **oxidative phosphorylation** takes place. On elementary bodies, the occurrence of a binding factor (protein) between electron transport and oxidative phosphorylation is assumed. Between the outer and inner membranes is the **intermembrane space**.

# Matrix

Mitochondrial cytoplasm is often called the **mitochondrial matrix**. It contains the circular mtDNA molecule and the proteosynthetic apparatus (very similar to prokaryote). Furthermore, a wide range of enzymes necessary for obtaining energy by oxidizing glucose is present. This includes, for example, enzymes of MK metabolism, pyruvate, and the Krebs cycle (e.g., transaminases, glutamic acid dehydrogenase and others). In the electron microscope, it has a homogeneous or granular appearance. It fills the space under the inner membrane, in which the electrodense areas - **intramitochondrial granules** - are stored with an average size of 20–50 nm, which are a morphological expression of calcium accumulation in the form of calcium phosphate. Their main components are phospholipids and bound inorganic material such as calcium, magnesium, phosphorus, strontium and barium. The size and number of granules is variable.

**Ribosomes** were discovered in the mitochondria , which, unlike the cytoplasmic ones, contain other enzymes that activate amino acids, and there is also a difference in tRNA.

# mtDNA

An important difference between mitochondria and other organelles is the fact that mitochondria are capable of **self-reproduction regardless of cell division**. The circular chromosome of mitochondria contains an **incomplete mitochondrial genome**. It is formed from a circularly arranged double-stranded DNA molecule and no histone-type proteins are bound to it. It codes for proteins of the respiratory chain, the Krebs cycle and several others. But it does not contain all genes, some have moved to the nucleus of the cell. It is inherited by a special matroclinic inheritance that does not follow Mendel's laws. In clinical contexts, rare but serious mitochondrial diseases are important.

🔎 *For more information see Genetic makeup of mitochondria.*

# Mitochondrial disease

Mitochondrial diseases are conditions caused by a malfunction of the mitochondria. They can be both acquired and congenital.

## Causes of disease

### Congenital

Inherent causes of mitochondrial diseases are errors (mutations) in sections of nuclear or mitochondrial DNA (so-called mtDNA, see above) that affect their activity. Mitochondrial DNA mutates more often than nuclear DNA. If all mtDNA molecules are affected, we are talking about a so-called homoplastic disorder, if some mtDNA molecules

are without mutation and others are not, this is so-called heteroplasty (if more than 80% of all mtDNA molecules are affected, this is already a very serious heteroplasty). Mutations in mtDNA usually affect the function of the respiratory chain or the Krebs cycle.

#### Obtained

Acquired disorders can be the result of infection, negative environmental influences or the use of certain medications. We usually observe disorders in mitochondrial metabolism, with oxidative phosphorylation disorders being the most frequently described.

### Symptoms

Mitochondrial defects are usually observed clinically as various degenerative diseases (brain, heart or skeletal muscles). With simultaneous damage to the muscles and the brain, we speak of so-called encephalomyopathy. Mitochondrial disorders can also be manifested by improper function of the kidneys or endocrine glands.

🔎 *For more information see Genetic makeup of mitochondria.*

## Function

The main function of mitochondria is the production and release of energy for the needs of the cell in the form of ATP (respectively ADP phosphorylation). This function is carried out by mitochondria through a system of biological oxidations. Mitochondria also regulate cellular metabolism and perform a number of other functions.

### Energy production

Carbohydrates (glucose). are the most important source of energy for heterotrophic organisms. By oxidizing them to water and carbon dioxide, energy is obtained in the form of ATP. It is a rather complex process, consisting of many sub-reactions and taking place in different places of the cell. Part of these reactions takes place in the mitochondria as the so-called Krebs or citrate cycle.

In aerobic cells, **glucose oxidation can be divided into three stages**. (In doing so, we assume a sufficient supply of oxygen to the organism, otherwise the process of splitting glucose - see glycolysis - would be followed by fermentation. The fermentation process is independent of mitochondria, but its energy yield - ATP - is significantly poorer than during classical cellular respiration.)

#### Glycolysis

First, the so-called glycolysis takes place (glyco = sugar, lysis = splitting). Six-carbon glucose is split into a three-carbon compound - pyruvate (one molecule of glucose to two molecules of pyruvate). Enzymes, that mediate this reaction are located in the cytoplasm of cells. The reaction takes place under anaerobic conditions. Thanks to this reaction, two molecules of ATP will be released. If the cell has enough oxygen, pyruvate is moved (this is active transport, two ATP molecules are consumed) from the cytoplasm through the mitochondrial membrane to their matrix, where it is oxidized to acetyl coenzyme A. (First, pyruvate reacts with coenzyme A to form carbon dioxide, NADH and acetyl coenzyme A).

#### Krebs cycle (also citrate cycle or citric acid cycle)

The previously mentioned Krebs cycle continues in the mitochondrion environment. Enzymes of the Krebs cycle have been demonstrated mainly in the mitochondrial matrix, but some of them are embedded in the inner mitochondrial membrane. The sequence of reactions taking place in the Krebs cycle can be characterized as **the conversion of acetyl coenzyme A into carbon dioxide and water with the simultaneous formation of ATP** (two molecules per one molecule of acetyl coenzyme A) and reduced coenzymes, which represent the source of electrons in the respiratory chain (three molecules of NADH and one molecule of FADH2 per one acetyl coenzyme A). The course of the Krebs cycle can be divided into three phases:

- acetyl coenzyme A and oxaloacetate react together to form citrate
- this molecule is subsequently shortened by two carbon atoms, which are subsequently oxidized to carbon dioxide
- eventually, oxaloacetate is regenerated and another molecule of acetyl coenzyme A can enter the cycle

#### Respiratory (electron-transport) chain

Mediation of the so-called respiratory chain is another step in obtaining energy for mitochondria. Enzymes and metabolites of the respiratory chain are located in the inner mitochondrial membrane and pass from the matrix to the intermembrane space and back. This localization ensures the supply of reduced coenzymes (NADH and FADH2) from the Krebs cycle. Another source of reduced coenzymes is glycolysis taking place in the cytoplasm. The essence of the respiratory chain is the transfer of hydrogens from reduced coenzymes to elemental oxygen. This plot takes place in stages using several transmitters. The components of this chain are localized on membranes according to their increasing affinity for electrons. Energy is released by the transfer of hydrogens from reduced coenzymes to the oxygen of the respiratory chain. This is further used to phosphorylate ADP to ATP (one pair of electrons enables the phosphorylation of 3 ADP molecules). This process is called oxidative phosphorylation. Enzymes and other compounds that are involved in the process of oxidative phosphorylation are stored on

mitochondrial cristae on elementary globular particles. Peter Dennis Mitchell, who received the Nobel Prize in 1978 for the formulation of the so-called chemiostomy hypothesis, dealt with the transfer of hydrogens through reduced coenzymes and the transformation of this phenomenon into ATP synthesis. In this phase, an energy yield of 34 ATP molecules will occur.

The total gain during aerobic respiration is therefore 38 molecules of ATP, while it can be simply said that 2 molecules of ATP are consumed to move pyruvate to the mitochondria. The actual energy yield from one glucose molecule is therefore **36 ATP molecules.**

### Heat production

A significant amount of the protein **thermogenin** (discovered in 1973) can also be found on the inner mitochondrial membrane. We observe this phenomenon especially in adipocytes of brown adipose tissue (e.g. in newborns between the shoulder blades, in hibernating animals). Thermogenin makes it possible to "bypass" the process of oxidative phosphorylation, and the reflux of protons from the intermembrane space is used to produce a significant amount of heat. We use the term **non-tremor thermoregulation** for this event .

### Calcium ion storage

Mitochondria can also function as a storehouse of calcium (similar to the endoplasmic reticulum), thereby helping to maintain a constant internal environment in the cell (homeostasis).

### Beta-oxidation

The mitochondrial matrix also contains enzymes of ß-oxidation of fatty acids - **aerobic breakdown of fatty acids** in the mitochondria. Again, we are talking about a cycle of successive reactions, serving several purposes. One of the products is again **acetyl coenzyme A**, which can again be used to produce energy. In the course of ß-oxidation, reduced coenzymes are further formed, which are then used in the respiratory chain.

### Additional functions of mitochondria

- membrane potential regulation
- participation in cell apoptosis (controlled cell death)
- participation in steroid hormones synthesis (tubular-type mitochondria)

## Chemical structure of mitochondria

Mitochondrial membranes composed of lipoproteins (they are made up of 50-60% proteins and 40-50% lipids). About half of all proteins are structural proteins and the other half are enzyme proteins. It was found that the enzymes of the respiratory chain and oxidative phosphorylation are located in the mitochondrial membranes, while the enzymes of the Krebs cycle are bound in the matrix. The outer membrane, which is richer in phosphatides and cholesterol, is characterized by the presence of enzymes such as fatty acid thiokinase, monoamine oxidase, kynurenine hydroxylase and others. The inner mitochondrial membrane has less cholesterol. Contains enzymes of the respiratory chain, e.g. cytochrome oxidase, cytochromes and some dehydrogenases. In addition, oxidative phosphorylation enzymes, mainly ATP synthases and other dehydrogenases, are present here. Such enzymes are also found on the membranes of crystals.

## Links

- ws: Mitochondrie

### Related Articles

- Respiratory chain
- Energy system of the cell
- Genetic makeup of mitochondria
- Matroclinic inheritance
- Mitochondrial diseases
- Mitochondrial neurogastrointestinal encephalomyopathy

### External links

- MITOMAP – A human mitochondrial genome database (https://www.mitomap.org/MITOMAP)
- Mitochondria atlas (http://www.drjastrow.de/WAI/EM/EMMitoE.html)
- Mitochondrial Disorders Overview (https://www.ncbi.nlm.nih.gov/books/NBK1224/)
- Mitochondrial Physiology Society (http://www.mitophysiology.org/index.php/Mitochondrial_Physiology_Society)

### References


- NEČAS, Oldřich. *Obecná biologie pro lékařské fakulty.* 3. edition. H+H, 2000. ISBN 80-86022-46-3.

- KONRÁDOVÁ, Václava – UHLÍK, Jiří – VAJNER, Luděk. *Funkční histologie.* 2. edition. H & H, 2000. 291 pp. ISBN 80-86022-80-3.
- PROF. MUDR. KAROL KAPELLER, DRSC., – STRAKELE, CSC., Doc. MUDr. Helmut. *Cytomorfológia : Učebnica pre lekárske fakulty.* 1. edition. Vydavateľstvo Osveta, spol. s. r. o, 1999. ISBN 80-88824-79-6.
- LÜLLMANN-RAUCH, Renate. *Histologie.* 3. edition. Grada Publishing, a. s., 2012. ISBN 978-80-247-3729-4.
- F. PAULSEN, PHD., Douglas. *Histologie a buněčná biologie : Opakování a příprava ke zkouškám.* 4. edition. Nakladatelství H & H Vyšehradská, s. r. o, 2004. ISBN 80-7319-024-9.


## References


1. JUNQUIERA, L. Carlos – CARNEIRO, José – KELLEY, Robert O, et al. *Basic Histology.* 1. edition. Jinočany : H & H, 1997. 502 pp. ISBN 80-85787-37-7.