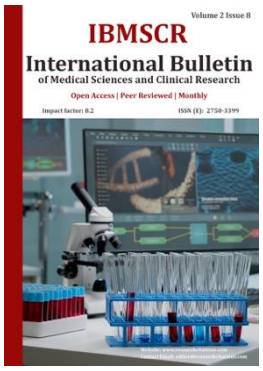

STRUCTURE AND FUNCTION OF MITOCHONDRIA: AS THE CENTER OF ENERGY PRODUCTION

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Abstract: This article provides comprehensive scientific information on the origin, structure, genetics, and function of mitochondria. Mitochondria are considered essential biological structures as the primary source of energy that ensures the vital activity of the cell. The study of mitochondrial structure and function is important not only for understanding cellular energetics but also for elucidating the mechanisms underlying the development of many diseases. This is because disturbances in mitochondrial function are closely associated with cardiovascular diseases, nervous system disorders, and numerous metabolic diseases. Therefore, an in-depth investigation of mitochondrial structure and functions is regarded as one of the most pressing directions in modern medicine and biology.

Keywords: mitochondria, membrane, matrix, mtDNA, ATP, glycolysis, Krebs cycle, oxidative phosphorylation, apoptosis, mitochondrial diseases.

Introduction: Every cell in the human body constantly requires energy. All processes occurring within the cell—growth, division, movement, respiration, and even the resting state—cannot proceed without energy. The most important role in energy production is performed by mitochondria. For this reason, they are often referred to as the "cellular battery" or the "powerhouse of the cell." However, their function is not limited solely to energy production. Mitochondria also play key roles in health and disease, in the regulation of apoptosis, in the synthesis of hormones such as steroids, and in maintaining intracellular communication at all levels through interactions with other organelles, the nucleus, and the external environment. Thus, mitochondria are regarded not merely as simple cellular organelles, but as critical systems that play a central role in sustaining the life of the entire organism. By studying mitochondrial function, it is possible to understand the causes of many diseases, their mechanisms of development, and potential preventive strategies.

Main Part: Mitochondria (derived from the Greek words mitos meaning "thread" and chondros meaning "granule") are important organelles located in the cytoplasm of the cell and are responsible for energy production. The energy produced by mitochondria is stored in a small molecule called adenosine triphosphate (ATP). Mitochondria are found in all eukaryotic cells, except in mature mammalian red blood cells. They are completely absent in bacteria and blue-green algae (cyanobacteria) [1]. In cyanobacteria, the process of energy production occurs directly on the cell membrane, which indicates that mitochondria appeared later in the course of evolution.

Mitochondria were first identified in 1894 by the German anatomist and histologist Richard Altmann, and in 1897 the German histologist Carl Benda named them mitochondria [2]. By the mid-20th century, following the invention of the electron microscope, the internal structure of mitochondria was studied in detail. The shape of mitochondria varies depending

on the cell type and its functional activity. In some cells, they are spherical or oval, while in others they appear thread-like or rod-shaped. During periods of increased energy demand, mitochondria elongate or fuse with one another to form larger structures. Conversely, when the cell is in a resting state, they contract and assume smaller forms.Mitochondria are dynamic organelles, meaning they are structures capable of changing their shape. The length of mitochondria usually ranges from 0.5 micrometers to 7 micrometers, but in some highly active cells this value may reach up to 10 micrometers [3]. Their shape and number are directly related to the cell's energy production needs.

For example, in muscle and cardiac cells, mitochondria are numerous and arranged in elongated, thread-like forms, as these tissues require continuous energy supply. In liver or kidney cells, however, mitochondria are more commonly oval or granular in shape.

In terms of number, unicellular eukaryotes usually contain a single mitochondrion; most animal cells contain approximately 150–1500 mitochondria; in female gametes their number can reach several hundred thousand; liver cells contain about 2,500 mitochondria; and in sperm cells there is a single giant mitochondrion spirally wrapped around the axis of the flagellum. In the human parasite Trypanosoma, a single branched mitochondrion is also observed [4]. The variability in shape and number allows mitochondria to adapt to the metabolic demands of the cell, making them among the most dynamic and active organelles within living cells.

Structurally, mitochondria are surrounded by a double membrane, which forms a boundary between the internal environment of the organelle and the surrounding cytoplasm. The outer and inner mitochondrial membranes differ in their chemical composition, enzyme content, and functions. The thickness of both the outer and inner membranes is approximately 70–80 Å, while the intermembrane space is about 100 Å wide [7].

Outer membrane:

The outer membrane has a smooth structure and consists of approximately 15% proteins and 85% phospholipids [4]. It contains transport proteins that facilitate the passage of intracellular molecules, including ADP, phosphate, and pyruvic acid. The outer membrane is semi-permeable and allows the passage of substances with a molecular weight of up to 10,000 daltons. Therefore, it plays a key role in regulating exchange processes between the mitochondrion and the cytoplasm.

Innermembrane:

The inner membrane consists of about 70% proteins and 30% phospholipids and has a much more complex structure than the outer membrane. Unlike the outer membrane, the inner membrane is highly selective and restricts the passage of molecules; therefore, entry of substances into the matrix occurs via specific carrier proteins. The inner membrane folds inward to form structures known as cristae, which greatly increase the surface area. These folds play a crucial role in energy production, as they are the sites where respiratory chain enzymes are located. Proteins embedded in the inner membrane carry out ATP synthesis (the process of oxidative phosphorylation). In addition, the inner membrane is essential for the formation of the proton (hydrogen ion) gradient [1].

Intermembrane space and matrix:

Between the outer and inner membranes lies the intermembrane space, which serves as a temporary reservoir for various substances. Inside the inner membrane is a gel-like substance

called the matrix. The matrix contains electron-dense, spherical granules with diameters of 20–40 nm, which include calcium and magnesium ions as well as polysaccharides such as glycogen, along with numerous enzymes [4]. The matrix also contains the Krebs cycle enzymes, circular DNA, and mitoribosomes (mitochondria-specific ribosomes).

Mitochondria are considered semi-autonomous organelles because they can independently perform certain processes without direct dependence on the nucleus, such as protein synthesis. The main reason for this is the presence of circular DNA molecules (2–6 copies) lacking histone proteins (similar to prokaryotic DNA), a set of tRNAs, mitoribosomes, and the enzymes required for protein synthesis. However, mitochondria are not completely autonomous: approximately 99% of the proteins and enzymes required for mitochondrial function are encoded by nuclear genes, synthesized in the cytoplasm, and subsequently imported into the mitochondria [5].The semi-autonomous nature of mitochondria is closely related to their evolutionary origin. According to scientific perspectives, mitochondria originated as a result of ancient prokaryotic cells adapting to life inside eukaryotic cells (the endosymbiotic theory) [6].

Therefore, mitochondria have retained several prokaryotic characteristics in both their structure and genetic apparatus.

Because mitochondria actively participate in cellular energy metabolism, their structure changes according to the metabolic demands of the cell. In other words, mitochondria do not maintain a constant form; instead, they can exist in two functional states depending on cellular energy requirements:

1. Inactive (or orthodox) state
2. Active (or condensed) state

Inactive (orthodox) state:

In this state, the mitochondrial matrix volume is relatively large, while the cristae are poorly developed. This condition is typically observed when cellular energy demand is low and ATP synthesis is not intensive [8]. Although mitochondria possess the necessary enzymatic components, they remain in a relatively inactive phase. This state is characteristic of resting cells or cells with slow metabolic activity.

Active (condensed) state:

In contrast, during the active state, the matrix volume slightly decreases, while the number and depth of cristae increase. The expansion of cristae increases the surface area of the inner membrane, which enhances the activity of respiratory chain enzymes and intensifies ATP synthesis [6]. This state is observed in cells with high metabolic activity, such as during physical activity, active growth, or tissue repair processes.

Mitochondrial DNA (mtDNA):

Within the inner region of mitochondria lies a distinct type of DNA known as mitochondrial DNA (mtDNA). This DNA has a circular structure and is significantly smaller in size compared to nuclear DNA [9]. mtDNA is primarily located in the matrix, where proteins involved in the electron transport process are active.

Human mtDNA contains 37 genes:

13 genes encode proteins directly involved in ATP synthesis via the respiratory chain,
22 genes encode transfer RNAs (tRNAs),
2 genes encode ribosomal RNAs (rRNAs) [6].

Thus, mtDNA mainly carries genetic information related to energy production processes, which explains the central role of mitochondria in supplying cellular energy.

One important characteristic of mitochondrial DNA is the absence of protective histone proteins. While nuclear DNA is protected by histones, mtDNA lacks such protective proteins [10]. As a result, mtDNA is more susceptible to damage caused by reactive oxygen species. The more intense the cellular energy production, the greater the generation of reactive oxygen species, thereby increasing the risk of mtDNA damage.

Mutations or alterations in mtDNA most commonly occur in tissues with high energy demand, such as:

cardiac muscle,

brain tissue,

skeletal muscle [11].

Because these tissues are constantly active and contain large numbers of mitochondria, mtDNA damage often leads to neurological disorders, muscle weakness, and cardiac dysfunction.

Therefore, mtDNA serves as a key source of genetic information essential for the stable functioning of energy-related cellular processes.

Mechanism of Energy Productio:

Mitochondria are considered the primary energy centers of the cell. Within them, energy is synthesized in the form of ATP through a multistep process. The initial stage is glycolysis, which occurs in the cytoplasm of the cell. During glycolysis, glucose is broken down into two molecules of pyruvate, producing a small amount of ATP [12]. Although glycolysis takes place outside the mitochondria, it provides essential substrates for subsequent stages of energy production. Therefore, glycolysis is regarded as one of the most ancient metabolic processes present in all living cells.Pyruvate subsequently enters the mitochondrial matrix, where the Krebs cycle begins. During the Krebs cycle, pyruvate is converted into acetyl-CoA, resulting in the formation of carbon dioxide and hydrogen carriers [13]. This cycle serves as a central hub of metabolic pathways, as many amino acids and lipids can also be processed through it. This highlights that mitochondria play a crucial role not only in energy production but also in maintaining overall metabolic balance.

The most important stage of energy production occurs on the inner mitochondrial membrane and is known as oxidative phosphorylation. During this process, hydrogen protons and electrons move along the electron transport chain, creating a proton gradient across the membrane. This gradient drives the synthesis of ATP by the enzyme ATP synthase [14]. The significance of this process lies in its ability to store energy in chemical form, thereby enabling the cell to sustain numerous vital functions.

In this way, an average of 36–38 ATP molecules are produced from a single glucose molecule. However, this value may vary depending on factors such as the physiological condition of the organism, oxygen availability, or a decrease in mitochondrial activity. For example, during physical exercise, the number and activity of mitochondria increase, which enhances the endurance of muscle cells.

Such a highly efficient system of mitochondrial energy production allows cells to function effectively under various conditions. Energy production can vary according to the body's state, oxygen levels, and metabolic demands. Therefore, when mitochondrial activity declines,

symptoms such as fatigue, muscle weakness, and nervous system disorders are often observed [15]. Organs with high energy demands—such as the brain, heart, liver, and muscles—are particularly dependent on mitochondrial function.

Other Functions of Mitochondria:

Mitochondria are not limited to energy production alone; they also play a vital role in regulating cellular life processes. First and foremost, mitochondria participate in apoptosis, the programmed and orderly process of cell death [16]. This process is essential for tissue renewal and the timely elimination of damaged or dysfunctional cells. Disruption of apoptosis can lead to excessive cell proliferation or, conversely, rapid tissue degeneration. Therefore, mitochondria are considered one of the key organelles that determine cell survival.

Another important function of mitochondria is the storage and regulation of calcium ions within the cell [17]. Calcium ions are critical for processes such as muscle contraction, nerve impulse transmission, and hormonal signaling. When cytoplasmic calcium levels increase, mitochondria absorb calcium and release it when necessary. This mechanism prevents excessive cellular excitation and helps maintain metabolic stability.

Mitochondria also participate in thermogenesis, the production of heat energy in the body. In certain specialized tissues, such as brown adipose tissue, mitochondria release energy directly as heat instead of producing ATP [18]. This process is especially important for newborns, animals living in cold environments, and for maintaining body temperature during exposure to cold conditions.

In addition, mitochondria are involved in the biosynthesis of steroid and certain other hormones [19]. The first step of steroid hormone synthesis from cholesterol occurs within mitochondria. This process is essential for endocrine glands such as the adrenal glands, gonads, and certain brain cells. Thus, mitochondria are not merely energy-producing organelles but also central regulators of the cell's metabolic and hormonal balance.

Mitochondrial diseases, their treatment, and the relationship between mitochondria and agingMitochondrial diseases are a group of chronic disorders that arise as a result of impaired cellular energy production and are mainly associated with mutations in mitochondrial DNA (mtDNA) or nuclear DNA [20]. They predominantly affect tissues with high energy demands, such as the nervous system, heart, liver, muscles, and eyes. Among the most common mitochondrial diseases are Leber's hereditary optic neuropathy, MELAS syndrome (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes), and Kearns–Sayre syndrome [21].

Leber's Hereditary Optic Neuropathy (LHON):

This disease is characterized by degeneration of the optic nerve. It most commonly occurs in men between 18 and 35 years of age. The underlying cause is defects in mitochondrial DNA, which prevent nerve cells from producing sufficient energy. As a result, patients experience sudden loss of central vision and impaired color discrimination [22].

MELAS Syndrome (Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes)

MELAS syndrome is characterized by energy deficiency in the brain and muscle tissues. Patients typically present in childhood or adolescence with symptoms such as muscle weakness, seizures, headaches, and visual and hearing impairments.

The term “lactic acidosis” in the disease name reflects a shift from ATP production to anaerobic glucose metabolism due to mitochondrial dysfunction, leading to excessive accumulation of lactic acid in the body [23].

Kearns–Sayre Syndrome (KSS)

This is a severe hereditary disorder caused by large deletions in mitochondrial DNA. It usually begins in childhood or adolescence. The main clinical features include ptosis (drooping of the eyelids), optic nerve atrophy, muscle weakness, cardiac conduction abnormalities, and endocrine disturbances [24].

Treatment of mitochondrial diseases remains a significant challenge due to the complexity of their genetic basis. Nevertheless, in recent years, mitochondria-targeted therapies have been actively investigated. For example, mitochondria-targeted antioxidants such as MitoQ and SkQ1 reduce cellular damage by neutralizing free radicals [25]. In addition, novel biotechnological approaches, including gene therapy and mitochondrial DNA transplantation, although still in experimental stages, hold great promise for future treatment strategies [26].

A decline in mitochondrial function contributes not only to disease development but also to the acceleration of aging. Studies have shown that with advancing age, mutations accumulate in mitochondria, their efficiency of energy production decreases, and this process represents one of the key molecular mechanisms of cellular aging [27]. Therefore, maintaining a healthy lifestyle, engaging in regular physical activity, and consuming an antioxidant-rich diet play an important role in preserving mitochondrial function.

Conclusion: Mitochondria can be regarded as the “heart” of the cell. They not only generate energy but also play a critical role in regulating overall cellular life processes. Due to their double membrane, their own DNA, and their semi-autonomous nature, mitochondria are distinct from other organelles. The energy produced by mitochondria serves as the driving force for all biological processes. Today, mitochondria are viewed not only as energy-producing organelles but also as components of the cell’s defense system, signaling pathways, and regulators of growth processes. They also play an important role in aging and in the development of various diseases. Therefore, ongoing research on mitochondria opens vast opportunities for the future in preserving human health and developing novel therapeutic approaches.

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