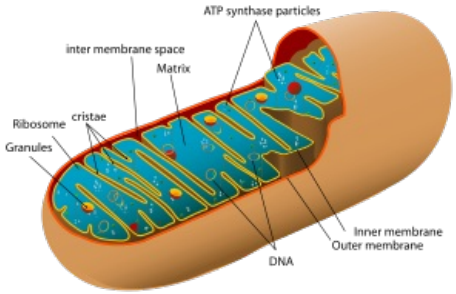
The importance of mitochondria in cell death and aging

Significance of mitochondria in necrosis



Mitochondria and its parts

In the early phase of necrosis, cell membranes are disrupted, causing the cells and their organelles, such as mitochondria, to swell and subsequently leak internal contents into the environment. This will cause the cell to break down.

Calcium homeostasis is impaired. Ischemia and some toxins are able to induce a very rapid increase in cytosolic calcium concentration through the flow from mitochondria, the endoplasmic reticulum and the extracellular space. This non-specifically increases the permeability of cell membranes and activates a number of enzymes that damage cell structures (especially phospholipases, proteases, ATPases, endonucleases).

This is followed by the loss of mitochondrial pyridine nucleotides, followed by a significant decrease in ATP and a reduction in the impossibility of its recovery. This disorder is due to ischemia and some pollutants and affects the integrity of the plasma membrane. High-energy bonds in the form of ATP are necessary for a number of synthetic and degradation processes.

Hypoxia acts on aerobic respiration, ie oxidative phosphorylation in mitochondria. The reduction in oxygen tension leads to a slowing down of oxidative phosphorylation and thus to the reduction of ATP production. This is followed by activation of anaerobic glycolysis and glycogenolysis, which results in the accumulation of lactate and an increase in inorganic phosphate content (hydrolysis of phosphate bonds). The intracellular pH decreases and chromatin is "clamped".

ATP depletion further leads to Na / K-ATPase disruption and thus to an isoosmotic increase in water content in the cell and cellular edema. Persistent hypoxia causes hyperhydration of the cell and mitochondria and then vacuolation of mitochondria and other membrane damage.

Oxidation in mitochondria produces reactive oxygen species (ROS). The postischemic increase in ROS is caused by an imperfect reduction of oxygen in the mitochondria and in the xanthine oxidase reaction, when superoxide and other ROS are formed.

The importance of mitochondria in apoptosis

There are two signaling pathways leading to **apoptosis** - internal and external.

The internal signaling pathway mediates most proapoptotic signals that originate mainly from the mitochondria. It is controlled by the interaction of two factors, the Bcl-2 family and Bax / BH3, depending on which signals the family predominates. The **external signaling pathway**is triggered by the activation of the lethal domains of the TNF receptor superfamily.

Mitochondria play an important role during the apoptosis signaling pathway because they can release cytochrome C. One of the putative mechanisms of apoptosis is alteration of the mitochondrial membrane. The inhibitory signal regulates the function of the mitochondrial channel for water and ions. Its suppression causes the inability of the channels to maintain a normal ionic potential between the inside and outside of the mitochondria. The collapse of the transmembrane potential increases the permeability of the mitochondrial membrane by opening its pores and thus swelling of the mitochondria. This swelling mainly affects the inner mitochondrial membrane, as it has a larger surface area, which in turn causes ruptures of the outer membrane, disruption of the [respiratory chain] and release of cytochrome C from the intermembrane space. Thus, even though cytochrome C is necessary for cellular respiration, it participates in its destruction.

There are two different theories of the release of cytochrome C from mitochondria:

- The opening of the mega-channel MPTP (permeability transition pore) will allow the penetration of solutes and water into the mitochondria and the already mentioned rupture of the membrane with all the consequences. However, this theory is not able to explain all forms of apoptosis, as sometimes mitochondria can remain unchanged.
- The second theory assumes no major disruption of the outer membrane, but the formation of channels that will allow the transfer of cytochrome C with the participation of VDAC and the channel protein Bcl2.

Importance of mitochondria in aging

As **aging** , the oxidative phosphorylation capacity gradually decreases and pleomorphic vacuolation of mitochondria occurs. ROS are caused daily by base alterations in both DNA and mtDNA, while the possibilities of a corrective mechanism, whose abilities decrease with age, are gradually being exceeded. Thus, mtDNA is progressively more damaged. This thesis is evidenced by radical / mitochondrial abortion theory.

Odkazy

Související články

- Stárnutí organizmu

Použitá literatura

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Source

- ws:Význam mitochondrií v buněčné smrti a stárnutí