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The Role of Mitochondria in Cellular Processes

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In this review is discussed mechanisms of mitochondria participation in programmed cell death mechanisms. The mitochondria are main unit, integrating signals that activates different ways of programmed cell death: apoptosis, autophagy, and necrosis-like programmed cell death. It is assumed that at mitochondria participate in a «choice» of cell death way. The integration of different mechanisms of cell death predetermines the possibility mitochondria use as one of main objects of cell protection from different death stimula.

KEYWORDS: mitochondria, apoptosis, autophagy, and necrosis-like programmed cell death

I. INTRODUCTION

It is currently difficult enough to assess the value of dysregulation of the programmed cell death (PCD) in the development of various pathological processes. To date, three forms of PCD are known: apoptosis, autophagy and necrosis-like PCD. Activation of cell death is one of the main mechanisms of cell loss in the affected organs and tissues of the pathological process, which contributes to the development of structural and functional disorders. As an example can lead to an increase in the activity of programmed cell death in tissues after ischemia and reperfusion (heart attacks, strokes), with neurodegenerative diseases in processes myocardial remodeling, erosion and rupture of atherosclerotic plaques, during the formation aneurysms, development of fibrotic changes in pancreas, pancreatitis and many other pathological their processes.

Found that the main component, was those who perceive the stimuli of the PCD and the endorsing mechanisms for the implementation of one or another forms of PCD are mitochondria. The assumption it is believed that at the level of mitochondria, integration of signals activating and suppressing the process of PCD, the consequence of which is further implementation of the programmed cell death or its suppression. Studying these molecular mechanisms governing these processes, will open up new perspectives for creation of technologies for the protection of tissues and organs from uncontrolled cell death, associated based on the development of the above-considered illnesses.

Main ways of implementation programmed cell death

As of today, the existence of three main forms of programmed cell death: apoptosis (type I PCD), autophagy (type II PCD), necrosis-like PCD (type III PCD). Each of these types of cell death is characterized by natural biochemical, molecular and morphological features [1].

With apoptosis, a decrease in cells is observed in volume, condensation of chromatin and fragmentation of DNA into oligonucleosomal fragments. Mitochondria and ribosomes during implementation apoptosis retain mainly their structure and partially - functions. The final stage of apoptosis is characterized by destruction of the cytoskeleton, which leads to cell shrinkage and its fragmentation mutations to apoptotic bodies absorbed macrophages or other neighboring cells [1]. Key participants in the terminal phase apoptotic programs are cysteine proteases - caspases that carry out degradation of protein structures of the cell and activating nucleases. To additional effectors apoptosis inducing factor (AIF) [1].

Autophagy is characterized by swelling of mitochondria and cisterns of the endoplasmic reticulum, enlargement of the Golgi apparatus, sequestration cellular organelles by autophagic vacuoles, condensation of



chromatin and collapse of the nucleus. Components of the cytoskeleton in autophagy perform a key role in the uptake of cytoplasmic structures by lysosomes and persist for the entire process of cell death. The final stage of autophagy is the destruction of cell organelles with lysosomal enzymes, the result of which is cell degradation. After the implementation of autophagy, cellular debris is absorbed by neighboring cells. Fundamental performers of the autophagic program are lysosomes that carry out degradation captured by them cell organelles in the middle by the content of hydrolases - proteases contained in them (cathepsins), lipases and nucleases [12].

During the realization of necrotic cell death there is a significant swelling of mitochondria and endoplasmic reticulum, cessation of cytoplasmic circulation by autophagic vacuoles, the destruction of lysosomes and the release of contained enzymes into the cytoplasm, degradation of cytoskeleton and the destruction of the nucleus. The final event in this process is the rupture of the plasma membrane that promotes the effusion of cell contents into the intercellular space, which contributes to the induction of an inflammatory response. The necrotic form of PCA is characterized by participation of a wide variety of hydrolytic enzymes: caspases, endonuclease G, cathepsins, released from lysosomes, Ca²⁺ dependent proteases - calpains [1].

It has been shown that in the affected pathological process of tissue is possible induction of all previously considered cell forms of death. Ratio of different types of PGC may vary depending on type and strength of the impact of a stimulus that activates PGC. For example, the process of autophagy is more characteristic of neurodegenerative diseases associated with the formation of intracellular deposits of defective neurospecific proteins. In the myocardium, after ischemia and reperfusion, the necrotic form of PCA will prevail over apoptosis in areas of tissue that have undergone more strong effects of hypoxia [8].

Currently discovered intermediate new forms of cell death, combining in signs of one or another type of PCD: apoptosis and autophagy, apoptosis and necrosis [9]. All over its admissibility, this is determined by some generality of molecular mechanisms of induction, possibly their "intersection" and simultaneous activation of various programs of the cell.

Mechanisms of participation of mitochondria in the programmed cell death

Currently, mitochondria are considered the main link integrating various signals that activate and suppress the programmed cell death. An important feature of these organelles is the ability to know significant amplification of the effects emanating from them which activate the PGC.

It has been shown that the discovery of mitochondrial pore is a common point in the implementation of the mechanisms of all the above-discussed forms of PCD (fig. 1) [2]. Pore formation in mitochondria during leads to the exit of cytochrome C from mitochondria, which leads to the formation of apoptosome and active caspase. This process is the foundation mechanism of apoptotic cell death. Through open pores in mitochondria into cytoplasm factors are also released, they move forming into the nucleus and activating the implementation of PGC by caspase-independent mechanisms: endonuclease G and AIF, which binds DNA and activates nucleases and proteases in the nucleus. It is shown that the data factors are involved in development as apoptosis and necrosis. In addition to activators of cell death, mitochondria also release inhibitors of PCD (Smac / DIABLO, Omi / HtrA2) and caspase precursors (procaspase 2, 3, 9) [1]. To non-protein mediators of cellular death include Ca²⁺ ions, which activate when their release into the cytoplasm of calpain and Ca²⁺ dependent lipases, which leads to the implementation of necrotic form of PCA. Additional factor induction of PGC is an increase in production components of the mitochondrial respiratory chain reactive oxygen species that activate at low levels of apoptosis, autophagy and necrosis.

Mitochondria are known today as apoptotic pores (mitochondrial apoptotic pores - MAP) and pores with increased permeability transition pores - PTP). The mechanism of apoptotic pore formation in mitochondria is an oligomerization of proteins on the mitochondrial membrane Bax and Bak. PTPs are formed by combining into a single complex of ATP ADP antiporter (adenine nucleotide translocase, ANT), localized in the inner mitochondrial membrane, cyclophilin D located in the mitochondria, and porin (voltage dependent anion channel, VDAC) - the ion channel of the external mitochondrial membrane [4].

The process of pore formation in mitochondria is under the tight control of various regulatory systems of the cell. It was found that the formation of MAP due to oligomerization of Bax and Bak promoted by proteins inducers of PCA of the Bcl family 2: Bax, Bak, Bok, Boo, Bcl G, Bcl B, Bcl 2, Bad, Bim, Bmf, Bid, Noxa, Puma, BNip3. Prevention



MAP education is carried out by a representative mi family Bcl 2, neutralizing the effect of inductors of PGA (Bcl 2, Bcl xL, Bcl w, Mcl 1, Bcl B). PTP permeability is regulated by means of interaction of Bax with the main com PTP components: ANT and VDAC [10]. Determined that BNip3 and active poly (ADP ribose) polymerase 1 (PARP 1) induce the opening of PTP, which is accompanied given by a decrease in mitochondrial potential and an increase in the production of active forms of acid kind [3, 7]. It has been shown that benzodiazepine re receptors, hexokinase and creatine kinase can to determine the permeability of PTP [13]. Education mitochondrial pores possible by means of action on the mitochondria of cytoplasmic Ca²⁺ ions and reactive oxygen species. Action free radicals and Ca²⁺ ions consists in destabilization of mitochondrial membranes by means of activating them, respectively, about LPO or phospho-mediated lipolysis folipase A2. It has been established that damage to mi tochondria and the development of their functional disorders niy in various pathological processes and toxic damage to these organelles so it also contributes to the activation of Freight One through the mechanisms discussed above [2].

Thus, in addition to providing cells energy, mitochondria take an active part state in the processes of regulation and implementation of the program caused cell death, which increases the knowledge the study of these cell organelles in the development of different pathological processes.

II. CONCLUSION

Thus, mitochondria are one of the key intracellular components, taking participating in the regulation of programming processes bathroom cell death: apoptosis, autophagy and necro goose-like PCD. It has been found that mitochondria have a wide range of protein (cytochrome C, endonuclease G, AIF,) and non-protein factors (Ca²⁺ ions, reactive oxygen species), active the process of cell death after releasing driving them into the cytoplasm. These organelles are the way we integrate intracellular stimuli, induction circulating and blocking PGCs and repeatedly increasing shedding signals that activate cell death. Interesting from the point of view of pathological physiology logic is the possibility of PHC induction by mitochondria not only after being perceived outside new incentives, but also due to functional disturbances in these cell organelles. In the present there is still a reasoned hypothesis for, suggesting that the accumulation of violations in mitochondrial genome and MI progression tochondrial dysfunction is one of the mechanisms of aging of the body and the development of various pathological processes. Activation of Freight One under the influence of mitochondrial dysfunction is one of the pathogenetic mechanisms of development structural and functional disorders at the time organs and tissues affected by the pathological process yah. Regulation of at the level of mitochondria "choice" of the form of PCA, due to the ambiguous effect of various forms of PCA on tissue structures. Intersection times personal mechanisms of PCD in mitochondria predis shares the possibility of using mitochondria in as one of the key objects of protection cells from exposure to various damage factors: toxic damage, ischemic mia and reperfusion, oxidative stress and other their impacts.

Further study of the role of mitochondria in mechanisms of programmed cell death will contribute to a more coherent pictures of many pathological processes, asso triggered with the activation of cell death, which will be the basis for creating new original biomedical technology professionals lactics and treatment of these diseases.

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